# The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 114, NO. 21 — COPYRIGHT, 1940, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — MAY 25, 1940


## HEMANGIOMAS OF THE SKIN


GRANT E. WARD, M.D.
AND
E. EUGENE COVINGTON, M.D.
BALTIMORE


Our object in this paper is to record our observations and results of present day methods of therapy in the treatment of ninety-four consecutive cases of superficial hemangiomas representing 127 lesions. All of the material used for this paper is from the Oncology Clinic of the University of Maryland School of Medicine and Hospital. This work covers an eight year period, i. e. from the opening of the Oncology Clinic in the fall of the year 1930 to the end of the year 1938.

In a study of several hundred papers in recent current medical literature dealing with hemangiomas, we found that few authors gave details of therapeutic technics and actual statistics of results. Here we report carefully prepared statistics and show that even though radium irradiation usually gives the best results of any form of therapy, there have been times when the cosmetic results were not entirely satisfactory. This percentage of unsatisfactory cosmetic results is small and may be present with any form of treatment. It is to be recalled that surgical excision is not without scarring, the amount of surgical scar varying, of course, with the skill of the operator and the amount of tumor removed. When large hemangiomas are excised, some tension is put on the skin edges with a resultant wide scar. Large hemangiomas may also require two stage operations for complete excision. In considering cosmetic results one must give an honest evaluation of all forms of therapy as related to the resulting scar in comparison with the original size of the lesion and the disfigurement.

### INCIDENCE AND LOCATION

The most frequent location for superficial hemangioma is the nape of the neck. This is the commonly seen naevus simplex or telangiectasia nuchae of newborn babies. According to Blaisdell [1] a careful routine physical examination will show this type present in about 33 per cent of all newborn babies of the white race. We have not noticed this condition so frequently, but there is no doubt that it is common. These lesions usually are small and patchy in distribution, disappear easily on pressure, are never elevated, are pale red, and therefore do not impress the average observer as hemangiomas. A routine physical examination of adults often shows these reddened areas about the hairline of the neck even though the person was never aware of the mark. As a result no treatment is necessary, and such hemangiomas will not be considered further in this paper.

The second most common location for superficial hemangiomas is the head. In this series of 127 hemangiomas the lesions were found on various parts of the head in the following order of frequency: face 28.2 per cent, scalp 11 per cent, lip 11.8 per cent, neck 3.9 per cent (exclusive of telangiectasia nuchae) and eyelid 2.3 per cent; therefore a total of 57.2 per cent of all hemangiomas were about the head. The face was also the most frequently selected site for port wine stains (naevus flammeus), which occurred in 5.3 per cent of this series. This is unfortunate, for such hemangiomas give the poorest results with any form of therapy.

Hemangiomas appeared on the body and extremities as follows: chest 7.1 per cent, extremities 15.7 per cent, abdomen 3.9 per cent, back 12.6 per cent, vulva 1.5 per cent, scrotum 8 per cent, buccal mucosa 8 per cent.

We record here the twentieth case of hemangioma of the scrotum. It was a typical hemangioma, 0.5 cm. in diameter and elevated 0.2 mm., it disappeared easily on pressure, and it was not associated with the underlying contents of the scrotum. The nineteenth was reported by Gibson,[2] who brought the literature to date. Our patient was treated successfully by solid carbon dioxide.

In 55 per cent of the cases the hemangioma was single, but in 45 per cent there were two or more, a rather high percentage of multiple lesions. The association of superficial hemangioma with hemangioma in some internal organ has been reported many times, especially in pediatric and neurologic literature, the most common association being hemangioma of the face with hemangioma of the brain. Our series does not agree with the literature in this regard.

### CLINICAL CHARACTERISTICS

Three fourths of the superficial hemangiomas were present at birth, but an appreciable number did not appear until one or two months later. Hemangiomas seldom develop in infants after the first year, and thereafter the frequency decreases with age. It is unusual to see a hemangioma begin in an adult. The port wine stains were all present at birth.

Port wine stains usually remain of the same size and intensity of color noticed at birth except that they grow as the child grows, but there are a certain number of the cavernous and capillary hemangiomas which will increase in size and become more pronounced in color. Three cases of hemangioma of the extremities in this series enlarged after birth. The importance of this increase in size after birth is to be emphasized, as early


From the Oncology Clinic, Department of Surgery, University of Maryland School of Medicine and Hospital.


1. Blaisdell, J. H.: Vascular Nevi and Their Treatment, New England J. Med. 215:485-488 (Sept. 10) 1936.

2. Gibson, T. E.: Hemangioma of the Scrotum, Urol. & Cutan. Rev. 41:843-845 (Dec.) 1937.

treatment may prevent this growth. Only one case in this series extended laterally after radium treatment (fig. 6 *A*).

In the present series 90 per cent of the hemangiomas were in the white race and 10 per cent in the Negro race; 35 per cent were in males and 65 per cent in females. We believe that more blonds have hemangiomas than brunets, although we have found no statistics in the literature to substantiate this observation.

## TREATMENT

*Optimal Age.*—Treatment should be instituted as early as possible. It is better to begin before the child is 3 months old, but certainly before the end of the first year. Early treatment is recommended mainly for three reasons: 1. The endothelial cells lining the vascular spaces of the tumor are more radiosensitive during their embryonic and early life. The radiosensitivity of these cells decreases in direct proportion to age; therefore the good results from irradiation decrease in the same proportion. Our observations correspond with those of Figi,[3] who had poor results with irradiation of hemangiomas about the face in young adults. He advocates either electrocoagulation or surgical excision with skin grafting when necessary for these failures of radiation therapy. 2. Early treatment will prevent most lesions from getting larger and spreading laterally. 3. Residual effects of irradiation, such as scarring and increased pigmentation, decrease as the years go on, making for better cosmetic results. The earlier the treatment, then, the earlier and better the result.

*Radium Technic.*—In our clinic new cases are seen by a surgeon and a radiologist to get an unbiased opinion of the proper therapy. More lesions were treated by external irradiation than any other method. Radium alone was used in 74 per cent of cases and roentgen therapy alone, or more often combined with radium, in 10 per cent. Our technic for radium therapy is as follows: The amount of radium is usually 100 mg. of radium element, the filter is 1 mm. of platinum, screened with aluminum foil and rubber or felt, the distance

Fig. 1.—A typical good result of radium, *A* before and *B* after treatment. No other form of therapy could equal this cosmetic result.

usually one-fourth inch (0.6 cm.), the time from two to two and one-half hours; therefore the dose is from 200 to 250 milligram hours. The platinum filter will remove all the caustic beta rays, and the aluminum foil and rubber will remove most of the secondary rays from the primary filter. This combination filter gives a shorter and more uniform wavelength. The radium plaque is made to suit the size and shape of the tumor, permitting the radiation to be equally distributed throughout the growth.[4] The same treatment is repeated every three or four months until the growth disappears. Large hemangiomas have to be marked off into several areas corresponding to the size of the radium plaque used, and each area is treated separately, overlapping being guarded against.

Fig. 2.—A typical hemangioma of the face, *A* before and *B* after radium treatment. No other form of therapy would give such a pretty cosmetic result.

The greatest effect from the irradiation will be seen within the first two months, followed by a slow but progressive fading for from four to six months. This slowness of effect is important to remember and, if kept in mind, will often prevent overirradiation. We prefer the minimum number of treatments which will give the optimum result, for the less irradiation used the less likely is sclerosis, atrophy, increased pigmentation or other abnormality to be left as a residual effect of overirradiation. One treatment was sufficient for 31.5 per cent of the 127 hemangiomas, but two and even three treatments were necessary for the remainder. Infants required fewer treatments than older children. With our technic of the radium element plaque, it is unwise to use more than two or three treatments to any one area because of the danger of late residual effects. When three such treatments fail to obliterate the growth with a good cosmetic result, some other procedure, usually excision, is used. Newcomet,[5] of Philadelphia, and many others emphasized that small doses of radium, especially in the beginning of treatment, repeated several times over a long period, give the best cosmetic results of any type of hemangioma therapy. In the future we intend to use smaller doses than those outlined, as experience has taught us that the reaction is often too pronounced. Slightly smaller doses, i. e. from 175 to 200 milligram hours, repeated three or four times, will probably cause less reaction with just as much disappearance of the lesion.

Irradiation, either by radium or roentgen rays, acts by producing obliterative endarteritis and a mild diffuse sclerosis of the surrounding stroma. The ultimate results depend on at least three factors: radiosensitivity of the tumor cells, size of the vascular spaces, and asso-

3. Figi, F. A.: Hemangioma of the Face, Proc. Staff Meet., Mayo Clin. **12**: 437-422 (July 14) 1937.

4. This dose over an area from 1 to 1½ inches in diameter usually produces an erythema in blonds and a suberythema in brunets in about seven to ten days. The University of Maryland Hospital has available 230 mg. of radium element distributed in tubes of 10 and 20 mg. strength, each with 1 mm. of platinum, and nineteen needles of 2, 5 and 10 mg. strength, each with a 0.5 mm. platinum filter.

5. Newcomet, W. S.: The Treatment of Nevi: A Review of Cases Treated During the Last Fifteen Years with Analysis of End Results, Radiology **22**: 684-693 (June) 1934.

ciated proliferation of connective tissue stroma. Each will be discussed separately.

*Radiosensitivity.*—By radiosensitivity is meant the amount and speed of response of tissues to the application of radium or roentgen rays. It is a complex biologic phenomenon depending on several factors, two of which every one has agreed on: (1) the radiosensitivity of the tumor cells and (2) the radiosensitivity of the surrounding stroma.

1. According to Cutler, Buschke and Cantril,[6] the radiosensitivity of tumor cells is separated into three forms: (*a*) inherent, (*b*) transient and (*c*) acquired.

(*a*) Every cell has a certain characteristic inherent radiosensitivity. We do not know much about this intracellular reaction but it is believed to be determined by the usual life history of the cell. Blood cells, especially lymphocytes, have a short duration of life; mesodermal cells, such as those of muscle, connective tissue or bone, have a longer duration of life, and nerve cells have the longest duration of life of any cells in the body. It is therefore easy to see that tumors developing from lymphatic tissue, i. e. in lymphosarcoma and Hodgkin's disease, are the most sensitive of all tumors to irradiation, while tumors developing from nerve cell origin, i. e. neuroma and neurogenic sarcoma, are the most resistant to irradiation. Lymphocytes are then the most radiosensitive cells, ovarian and testicular cells rank second, and hemangiomas probably about third. A hemangioma, then, is fairly sensitive to irradiation.

(*b*) By transient radiosensitivity is meant the cellular response during certain phases of the cell's life history. A cell is most radiosensitive during mitosis and this radiosensitivity decreases as the cell grows older.

(*c*) By acquired radiosensitivity is meant the alteration in the original, or inherent, radiosensitivity. Radiosensitivity is never increased during the life of a cell but it may be decreased by several factors, the most important of which is diminished blood supply. One way in which this may be brought about is by previous irradiation, which causes obliterative endarteritis and

Fig. 3.—Hemangioma, *A* before and *B* after radium therapy. Severe infection followed treatment and trauma caused by scratching. Note involvement of eyelids and lips, a problem difficult or impossible to handle by plastic surgery. Marked scarring and residual patches of hemangioma remain. This is a bad result, but no other form of therapy would do as well. Solid carbon dioxide and electrodesiccation are to be used on the remaining patches of hemangioma. Much of this scar will soften with age.

a mild diffuse sclerosis, thus reducing the blood supply. Each course of irradiation makes a tumor more and more radioresistant. This is true to a certain extent of hemangiomas but applies particularly to sarcomas and epitheliomas. The age of the individual is an important factor in determining acquired radiosensitivity, this being especially true with hemangiomas and to a lesser extent with sarcomas and epitheliomas. A hemangioma is most radiosensitive during the early months of life. The radiosensitivity decreases in direct proportion to the age of the individual. Radiosensitivity of heman-

Fig. 4.—Papillomatous type of hemangioma of the scalp, *A* before and *B* immediately after treatment by electrodesiccation, showing a typical good result of electrodesiccation when the tumor has a narrow base. The dark spot in *B* is gentian violet applied to the desiccated area to show the amount of scar.

gioma is low in older children (over 3 or 4 years) and in adults hemangiomas are radioresistant.

2. The second known factor about radiosensitivity is the response of the stroma to irradiation. The tissues which make up the stroma supporting the tumor are mesodermal in origin, consisting of connective tissue, muscle, blood vessels and bone. The cells of these tissues, with the exception of blood vessels, are more radioresistant than the cells of hemangioma, epithelioma or even sarcoma, except neurogenic sarcoma. An epidermoid carcinoma developing in the region of the pharynx or tonsil is more radiosensitive than the same tumor histologically developing from the lip or growing as a metastasis in bone. In each case the surrounding stroma is different. The pharyngeal wall contains much lymphatic tissue, which is radiosensitive, the lip is made up of less radiosensitive muscle and connective tissue, and bone is still less radiosensitive. This is true to a lesser degree in hemangioma. A hemangioma beginning on the skin certainly seems more radiosensitive than the growth located in subcutaneous tissues, muscles or bone.

We have noted that hemangiomas containing large amounts of fat and connective tissue, which are firm and do not flatten out on pressure, also do not entirely disappear following irradiation. This is to be expected, as fat and connective tissue are resistant to the action of gamma rays of radium or roentgen rays. The vascular spaces become sclerosed, as evidenced by the change in color and partial reduction in size, and there is improvement but never a complete cure. Fortunately this mixed type of hemangioma is uncommon. It might be well to consider surgical excision at the outset of treatment in such cases provided the lesion is located on a site where excision is easily carried out.

The ultimate results of irradiation also depend on the size of the vascular spaces making up the tumor. A capillary hemangioma is a mass of small embryonic blood spaces with a supporting stroma. This is the usual type found in the skin; it may or may not be elevated, does not pulsate, usually blanches easily on

6. Cutler, Max; Buschke, Franz, and Cantril, S. T.: Cancer: Its Diagnosis and Treatment, Philadelphia, W. B. Saunders Company, 1938, pp. 1-5.

pressure and is the most radiosensitive of all hemangiomas. The only difference between a capillary and a cavernous hemangioma is the size of the vascular spaces composing the tumor. A cavernous hemangioma, especially a large one, usually has one or more afferent and efferent vessels. These tumors often pulsate. Most large hemangiomas, subcutaneous hemangiomas and hemangiomas originating in internal organs, i. e. in the liver, spleen, tongue and muscle, are cavernous in type. Cavernous hemangiomas, as a general rule, do not respond quite as well to irradiation as the capillary group. Our explanation for the lesser effect of irradiation on cavernous hemangiomas is that the vascular spaces are too large to be readily obliterated by the doses of radiation usually employed.

In our experience naevus vinosus, or port wine stains, do not obey the usual laws of sensitivity to irradiation. Our results were poor with either radium or roentgen therapy, regardless of the age of the individual. Although port wine stains are capillary hemangiomas, we have no explanation as to why they do not respond to irradiation. They have no definite afferent and efferent vessel, usually are not elevated and do not pulsate. Of the present series 5.3 per cent were port wine stains, all of which were on the face.

Fig. 5.—*A*, the usual amount of scar for a good result in a fair-sized hemangioma of the arm. *B*, large cavernous hemangioma of the back. The photograph was taken on admission. The patient was treated with three radium applications. Infection followed. A year later there was still a large amount of hemangioma and scarring. Excision advised but refused. In this type irradiation reduces the vascularity and thus makes excision safer.

*Electrosurgery.* — Superficial electrodesiccation and interstitial electrocoagulation are the second most common forms of therapy used in our clinic. Twenty-five per cent of all cases in this series had electrosurgery, alone or combined with radiation therapy. It is used for very small hemangiomas, especially if they are elevated and have a narrow base, i. e. less than 0.5 cm. in diameter. Many of these were resistant to treatment by solid carbon dioxide. Electrodesiccation for superficial lesions leaves the largest scar of any type of therapy, especially when used in large growths, and is therefore justifiable only when the lesion is quite small.

Interstitial coagulation is used in cavernous hemangiomas that have not responded well to irradiation (fig. 7 *A*, *B* and *D*). In many of these cavernous hemangiomas there is a larger portion of the tumor in the subcutaneous tissues than on the surface (fig. 7 *D*). The extent of this subcutaneous involvement is outlined by the elevation and characteristic bluish discoloration. All the cavernous growths are first treated by one or more external applications of radium. Several months is required to obtain the full benefit of this irradiation, and then the residual hemangioma is treated by interstitial electrocoagulation (fig. 7 *A*, *B* and *D*). Because of location or large size, a few of these lesions are not suitable for electrocoagulation and excision is preferable. Radium makes these tumors less vascular and excision is safer. Our technic of interstitial coagulation is as follows: A very fine electrosurgical needle is inserted into the tumor and a coagulating current is turned on for approximately five seconds, or until the growth begins to look pale. This same procedure is done throughout the tumor, the needle insertions being equidistant and about 0.3 cm. apart. One such treatment is usually sufficient. The secret of success is a mild current which does not cause too much coagulation. This treatment is usually carried out under local anesthesia. Procaine hydrochloride anesthesia has the disadvantage that it causes edema of the tissues, an objection easily met by using a concentrated solution (2.5 per cent) and injecting at a 1 or 2 cm. distance, making a circular block anesthesia. The only complication of interstitial electrocoagulation is slough, which is always caused by overcoagulation and should be avoided. Experience is the best teacher in determining the optimum amount of coagulation necessary for a particular growth.

*Solid Carbon Dioxide* (carbon dioxide snow, "dry ice").—The third most common form of therapy we have used is solid carbon dioxide. It has won the favor of pediatricians throughout this country, but radiologists and plastic surgeons have been less enthusiastic about it. Solid carbon dioxide causes the disappearance of the growth by the production of obliterative endarteritis and mild sclerosis of the surrounding stroma. If overdone, i. e. when used over ten seconds at one time, it acts as a caustic and may produce ulceration. It acts more quickly than irradiation and can be used more often, but it is not as efficient as a sclerosing agent. We have used it only for capillary hemangioma. Its action is too superficial to be of much value for a cavernous growth. Solid carbon dioxide is applicable for three types of hemangioma: 1. It is used for the small capillary variety, i. e. less than 0.5 cm. in diameter. It is hard to concentrate radium element in a plaque or roentgen rays into an area of such small size without the risk of resultant sclerosis, pigmentation and skin atrophy from irradiation of larger extent than the original growth (fig. 6 *C*). Solid carbon dioxide has the advantage that it can be cut to the exact size and shape of the lesion before treatment so that the scar, if any, will be no larger than the original growth. 2. Solid carbon dioxide is used for any patchy area of residual growth around the margins of a hemangioma previously treated by irradiation. It is true that further irradiation in these cases might cause a disappearance of the remaining hemangioma, but with this added irradiation there is a possible danger of increasing the amount of scarring, atrophy or telangiectasis. 3. Solid carbon dioxide is used in several areas where irradiation is contraindicated or mechanically impossible. We here record the twentieth case of hemangioma of the scrotum. It was successfully treated by solid carbon dioxide. Obviously, irradiation over the scrotum in infants is not without question and may be open to criticism. Testicular tissue is known to be very radio-

sensitive. Although we feel that the amount of irradiation required to eradicate hemangioma of the scrotum is probably insufficient to damage the deeper lying testicle, until further work has been done to determine the radiosensitivity of an infant's testicle it would seem safer not to use this form of therapy for hemangioma of the scrotum. The redundance of the skin of the scrotum makes surgical removal relatively simple. Because of the inverse square law, damage to the ovaries would not be expected when treating hemangioma of the vulva. Solid carbon dioxide was much simpler to use in our case of hemangioma of the scrotum than surgical excision or electrodesiccation. It gave a nice result.

Solid carbon dioxide is used for almost all capillary hemangiomas about the eyelids, internal canthi, external canthi and adjoining regions (fig. 7 *C*). It is mechanically almost impossible to keep radium directly on these lesions because of the constant movement of the eyelids. The eye is very resistant to irradiation, especially in the mild doses given for hemangioma, but the possibility of radium damage must always be borne in mind. With adults it is quite possible to protect the eye with lead plates of various shapes and sizes, but this is obviously impossible to do with infants.

Our technic for carbon dioxide therapy consists of direct application for from five to ten seconds, repeated at intervals of two months until the desired effect is obtained. The only important complication is ulceration, which can usually be prevented by using less intense freezing, never lasting over ten seconds at one séance.

*Sclerosing Solutions.*—Our experience with sclerosing solutions is not sufficient to warrant accurate comment. Malkin [7] has been successful with this form of therapy for hemangioma of the eyelid. Andrews and Kelly [8] had satisfactory results in twenty cases. They claimed improvement even for port wine stains. It seems that a more extensive use of this agent is necessary before it can be accurately compared with other methods.

*Interstitial Radium.*—This has never been used in our clinic for hemangiomas. Where used, however, it has practically the same indications as outlined for interstitial electrocoagulation. Brown and Byars [9] advocate this type of therapy and have been successful with it. External irradiation is the best of all sclerosing agents, as the rays diffuse equally throughout all parts of the growth. We believe it is possible to give as much irradiation as is safe for a particular hemangioma by the external method without having to resort to radium element needles or radon seeds interstitially.

*Surgical Excision.*—This is probably the oldest form of eradication of hemangiomas. Many times it is the quickest way of eliminating the disfigurement, especially when the lesion is located in skin that can be easily closed, i. e. on the back, abdomen, chest and occasionally face. About the eyelids and lips, particularly when the mucosa of the mouth is involved, excision may necessitate extensive plastic procedures. Such measures are not without residual scarring. To obtain the best surgical cosmetic results in extensive cases, two or more operations may be required. Surgical treatment of hemangioma means hospitalization and general anesthesia, the latter not without some risk, slight to be sure. All this was avoided in 87 per cent of the cases by using proper irradiation or irradiation followed by touching up small areas with solid carbon dioxide, with cosmetic results comparable to surgical scars. In this series surgical excision has not been performed. In private practice we have had an occasional case which required surgical excision after irradiation.

*Port Wine Stains.*—Two cases of naevus vinosus, or port wine stains, were treated by radium alone or combined with roentgen therapy. This work was more or less experimental. There was usually some fading out of the redness, but as a general rule the results were unsatisfactory. The preferable treatment for port wine stains is surgical excision if possible, followed by skin grafting when necessary. We have not used ultraviolet irradiation, but in the hands of some men, notably Blaisdell [1] and McCollum,[10] it has given promising results. McCollum advises giving one erythema dose weekly for from four to nine months, using an air-cooled ultraviolet Kromeyer lamp. He reports 80 per cent of his patients well or much improved.

Fig. 6.—*A*, atrophy of skin and loss of hair following radium treatment. Hemangioma developed by the side of the original growth. Early treatment usually prevents this extension. *B*, infected hemangioma on the popliteal space, the result of recent irradiation and trauma from scratching. This will leave an unsatisfactory scar. *C*, patches of residual hemangioma, telangiectasis and scarring following three radium treatments and several applications of solid carbon dioxide. A typical poor cosmetic result. This will improve with age. *D*, residual patches of hemangioma of the forearm and mild scarring following radium therapy. A typical poor result from radium. Excision to follow.

### COMPLICATIONS AND RESIDUALS

The complications following radiation therapy are immediate (within two or three weeks) or late. The most important immediate complication is infection

7. Malkin, Boris: Treatment of Angioma of Eyelid by Injection of Sclerosing Solutions, Arch. Ophth. **10**: 578-584 (Oct.) 1936.
8. Andrews, G. C., and Kelly, R. J.: Treatment of Vascular Nevi by Sclerosing Solutions, Arch. Dermat. & Syph. **26**: 92-94 (July) 1932.
9. Brown, J. T., and Byars, L. T.: Interstitial Radiation Treatment of Hemangiomata, Am. J. Surg. **39**: 452-457 (Feb.) 1938.
10. McCollum, D. W.: Treatment of Hemangiomas, Am. J. Surg. **29**: 32-35 (July) 1935.

(fig. 6*B*). It was seen in a few cases of overirradiation, with blister formation, scabs and other features. It may also follow trauma to the growth. Infants often cause irritation by scratching a freshly irradiated area. Several patients in this series were infected and had ulceration on admission. All patients who have infection, with or without irradiation, are always left with more scar (fig. 3*B*).

There are several late residuals and they are present, in order of their frequency and importance, about as follows: (1) sclerosis, (2) telangiectasis, (3) residual tumor, (4) increased pigmentation, (5) atrophy of skin, (6) loss of hair, (7) chronic radium ulcerations and (8) epiphysial injury.

1. *Sclerosis.*—To a varying degree sclerosis of tissues follows practically all therapeutic doses of irradiation

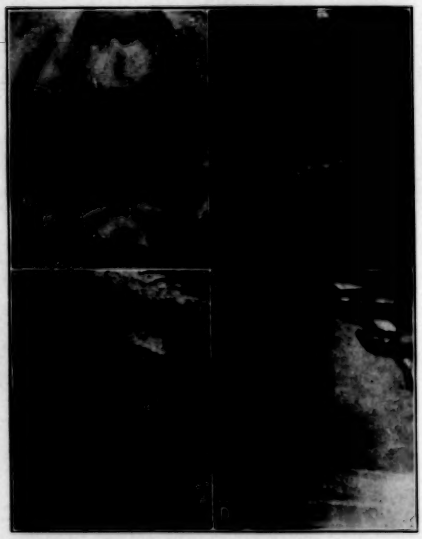


Fig. 7.—*A*, residual cavernous hemangioma of the lip following radium therapy. Interstitial electrocoagulation followed with a good result. *B*, the usual poor result of radium for adults. Interstitial electrocoagulation was advised but refused. *C*, typical hemangioma of the eyelid. Solid carbon dioxide or electrodesiccation is the proper therapy. *D*, a large subcutaneous cavernous hemangioma of the back after three radium treatments. Notice some residual growth present. Interstitial electrocoagulation is the proper treatment for this residual of subcutaneous hemangioma.

for hemangioma. Sclerosis is spoken of as a complication only when the scar tissue is thick and tough enough to give a poor cosmetic result. Sclerosis results from overirradiation, an insufficient filter or direct contact radium. One treatment of radium for hemangioma should never be above 250 milligram hours, preferably from 175 to 200 milligram hours, using the technic outlined previously. Beta rays from an insufficient filter, secondary rays from the primary filter, and direct contact radium are frequent causes of sclerosis; hence the importance of proper filtration. The scarring may be even or patchy. When present to such an extent that the cosmetic result is poor, excision is the proper therapy. It is the most common late residual but not particularly noticeable except in a few cases.

2. *Telangiectasis.*—This is a fairly frequent residual. In a general way the number of patients showing it is directly proportional to the quantity of radiation given. Our observations are that the quality of radiation makes no difference. It is often very difficult to distinguish between residual hemangioma and telangiectasis (fig. 6*C* and *D*). This is a very important differentiation because hemangioma needs more treatment, but further irradiation would very likely accentuate telangiectasis. As a general rule telangiectasis occurs around the periphery of a treated growth, the vessels have a spider web distribution, and it disappears poorly on pressure.

3. *Residual Tumor.*—Residual patches of hemangioma (figs. 3*B*, 6*C* and *D*) are a fairly frequent and very unfortunate complication. They may follow even after several radium treatments. Our explanation for this has been given in a previous paragraph. Residual tumor occurs more often in cavernous hemangioma than in the capillary form. Residual hemangioma in the capillary type of growth is treated by solid carbon dioxide and occasionally electrodesiccation, while residual patches in the cavernous type are treated by interstitial electrocoagulation. In a few of these cases surgical excision with skin grafting if necessary may give the best plastic result. This is one of the most important of all residuals.

4. *Increased Pigmentation.*—Increased pigmentation occurs to a slight extent in almost every case immediately after irradiation. The amount of pigmentation is generally in direct proportion to the amount of radiation given. This increased pigmentation fades out with time, the improvement being greater the younger the patient.

5. *Atrophy of Skin.*—Atrophy of skin may result from three causes: (1) pressure of the underlying tumor, (2) invasion of the skin by the proliferating blood vessels of the tumor, and (3) overirradiation. In many hemangiomas there is a mild degree of the first type of atrophy, occasionally sufficient to leave an appreciable atrophic scar. Overirradiation and an insufficient filter are the more common causes of skin atrophy. It occurred to a marked degree in only 1 per cent of this series (fig. 6*A*). Atrophy, of course, is closely associated with scarring. Almost every case of marked sclerosis will have a slight amount of atrophy.

6. *Loss of Hair.*—Loss of hair occurs immediately after every irradiation for hemangioma of the scalp. The hair usually returns after several months, but there are cases (2 per cent in this series) in which the hair over the treated area never returned (fig. 6*A*). The hair follicles were destroyed. From a fairly extensive review of the literature we were impressed by the fact that this residual effect of irradiation has not been stressed. It is important to bear this depilating effect of overirradiation in mind in planning treatment for hemangioma of the scalp. Probably milder treatments repeated over a longer period may prevent this complication. As a rule, such a bald spot is readily covered by the hair and is not noticeable.

7. *Chronic Radium Ulcerations.*—Irradiation ulcerations are uncommon complications. They occur from overirradiation, improper filters and secondary infections, or occasionally in a blond person whose skin is very radiosensitive. This has never occurred in our clinic, but a busy plastic surgeon will see it a few times every year. Davis and Wilgis [11] and many others have stressed the importance of irradiation injuries.

11. Davis, J. S., and Wilgis, H. E.: Treatment of Hemangiomata by Excision, South. M. J. 27:283-290 (April) 1934.

8. *Epiphysial Injury.*—Epiphysial injury with later disturbance in the growth of bone is an uncommon complication of irradiation. With proper irradiation by radium, the depth dosage is usually too small to cause epiphysial injury. High voltage roentgen therapy is more penetrating and will cause epiphysial injury, but the usual small doses used in treating hemangiomas should seldom cause permanent damage. We have not seen epiphysial injury in this series. Plastic surgeons, for instance Davis [11] of Baltimore, emphasize the possibility of this complication of irradiation.

## RESULTS

Every new patient who comes to the Oncology Clinic of the School of Medicine of the University of Maryland is seen by a radiologist and a surgeon for an unbiased opinion on the proper therapy. In discussing results we consider any and all forms of therapy, whether used alone or combined. Radium therapy is becoming more and more popular throughout the world, particularly in tumor clinics, and this has been by far our most common form of treatment.

Our results are classified as (1) good, (2) satisfactory, and (3) poor.

1. By a good result from radiation therapy is meant the entire disappearance of the tumor with no disfiguring patches of hemangioma, scarring, telangiectasis, atrophy, loss of hair, increased pigmentation, epiphysial injury or other residuals. It is to be remembered that some slight scarring remains after any form of therapy, but our definition of a good result is one in which the amount of scarring is no more noticeable than the fine linear scar following surgical excision. Of this series of ninety-four cases, all of which were superficial, the results were considered good in 40 per cent. The best results were obtained in infants below 2 years of age. After the period of infancy, the good results of irradiation decreased in direct proportion to age.

2. The results were satisfactory in 47 per cent of the cases. In this group also we compare the end results with what might have been accomplished by surgical excision. The reason for this comparison is that surgical excision is the older form of treatment for hemangiomas. Included in this satisfactory group are all cases in which there is a slight or moderate amount of scarring or telangiectasis, or small patches of tumor remain, or the tumor is entirely gone but the cosmetic result is only satisfactory. In this group too are placed many of the larger hemangiomas, especially of the face (fig. 3 *A* and *B*), where surgical treatment was out of the question because of the size of the growth or extensive involvement of eyelids, lips or nose. There has been a tremendous improvement in many of these cases, but obviously not a "good" result. In many of these cases the pronounced scarring (fig. 3 *B*) will improve with age, ultimately giving a more satisfactory result.

3. In the group yielding poor results (13 per cent in this series) are included: (1) all port wine stains (5.3 per cent), which are all radioresistant; (2) most hemangiomas in adults which were radioresistant and which were finally treated with electrosurgery or surgical excision, and (3) all cases in which the residuals, such as patches of tumor, telangiectasis, atrophy or loss of hair, were so pronounced that the cosmetic result was considered bad.

There are many who think that primary excision of hemangiomas without previous irradiation is the treatment of choice. They argue that time and expense will be saved by primary excision and that a cosmetic result equal to or better than irradiation will be obtained.[12] We contend that irradiation gives good or satisfactory results in a high percentage of cases (87 per cent in this series) and therefore that surgical treatment is unnecessary for the majority of hemangiomas. In many cases of failure by irradiation (fig. 6 *C* and *D*) surgical excision gives the same linear scar that primary excision would have given. The cavernous growths that have to be excised surgically are much less vascular and operation is safer if preoperative irradiation has been given.

## CONCLUSIONS

It is our opinion that as a general rule radium gives good results in a large percentage of cases of superficial hemangioma. A fairly extensive review of the literature on hemangiomas reveals that most articles deal with case reports of unusual types, successful cures by various methods of therapy advocated by many authors, and general discussions on the pathology of hemangiomas, but there was not much emphasis on the failures, complications and late residual effects of irradiation. The patients with bad results are commonly seen by plastic surgeons and do not return to the irradiation therapist unless carefully followed.

Radium has its greatest value for capillary and cavernous hemangiomas in young infants. Cavernous hemangiomas are treated best by external radium and, after several months, by interstitial electrocoagulation for the residual growth. External radium is by far the best and gives the most equally diffuse sclerosing effect of any of the sclerosing agents. Irradiation has given poor results in port wine stains.

Solid carbon dioxide is used for very small hemangiomas, residual patches of hemangioma, telangiectasis around the periphery of a lesion previously treated by irradiation, hemangiomas around the eyelids, and hemangiomas of the scrotum.

We believe that good results can usually be obtained in superficial hemangiomas, but only when the surgeon understands the indications, contraindications and limitations of all forms of treatment, including radium and roentgen therapy, the principles of good plastic surgery and electrosurgery. It is certain that a working knowledge of only one type of therapy will not give good results in all types of superficial hemangiomas.

214 Medical Arts Building.

12. The total expense of irradiation of hemangiomas is not comparable to the cost of hospitalization plus surgeon's fees. In private practice rarely is more than $25 charged for one treatment, and frequently the fee is less. A larger amount may be charged in cases of multiple hemangioma. We calculate radium overhead on a basis of 3 cents per milligram hour; an average treatment then would give an overhead of $7.50. Whatever is collected over this amount is considered as professional fee and varies with the financial status of the patient.

**History of Helium.**—Helium was discovered in the sun in 1868 by Jannsen and Lockyer by means of the spectroscope. Its existence on earth was demonstrated by Ramsay, who obtained it from the mineral cleavite. It was later found to be a constituent of the atmosphere to the extent of one part in 200,000. Recently it has been found to occur in certain natural gases. . . . In 1923 a patent was registered in the United States Patent Office by Charles Cooke for the use of helium with oxygen for divers, based on the fact that helium has a coefficient of solubility approximately half that of nitrogen, and because it is twice as diffusible. Sayers and Yant in 1926 decompressed animals from 10 atmospheres of helium-oxygen mixtures in from one-third to one-fourth the time necessary for nitrogen-oxygen mixtures and found no toxic effects from the use of helium under high pressures for short periods.—Barach, Alvan L.: The Therapeutic Use of Gases, chapter XIII in The Therapeutics of Internal Medicine, New York, D. Appleton-Century Company, Inc., 1940.

# THE DIAGNOSIS OF NEUROPATHIC JOINT DISEASE (CHARCOT JOINT)

## AN ANALYSIS OF FORTY CASES

RALPH SOTO-HALL, M.D.
AND
KEENE O. HALDEMAN, M.D.
SAN FRANCISCO

Although seventy years have passed since Charcot [1] described the type of joint disease which bears his name, physicians are still far from a complete understanding of its development. Its diagnosis is relatively simple if one bears in mind certain clinical and radiologic characteristics; yet the presence of a Charcot joint is frequently overlooked, especially in the early stages. The experiments of Eloesser,[2] who produced neuro-arthropathies in cats by traumatizing their joints after their limbs had been rendered anesthetic through the severance of the posterior nerve roots, confirm the usually accepted theory of pathogenesis that attributes the development of the Charcot joint to the effect of a single injury or repeated injuries on an articulation which

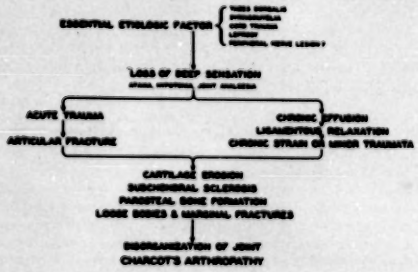



Fig. 1.—Evolution of a neuropathy.

has lost its sensibility to pain. Space does not permit an adequate review of the articles which have dealt with the clinical and pathologic aspects of neuropathic joint disease. Deserving special mention, however, are papers by Key,[3] Steindler,[4] Moritz,[5] Wile and Butler,[6] Knutsson [7] and Potts.[8]

Tabes dorsalis, though most frequently the underlying disease, is not the only condition which may lead to the development of a neuro-arthropathy. A similar loss of sensibility in the joint may occur in syringomyelia, injuries to the spinal cord and leprosy. The characteristics of a Charcot joint, in the order of their usual appearance, are an enlargement of the joint resulting from an effusion, a relaxation of its ligaments leading to instability and deformity on weight bearing, and thinning of the articular cartilages, marginal fractures, sclerosis of subchondral bone in some areas and atrophy of the bone in other regions, loose bodies in the joint, and the formation of new bone (parosteal bone) outside the joint cavity. Many of these later features are demonstrated by roentgenograms. The most striking clinical observation is the absence of pain in the presence of such an advanced pathologic process. The foregoing series of changes may be initiated by a fracture in a joint which appears normal. The observations and theories which explain the evolution of a neuro-arthropathy are best shown diagrammatically (fig. 1).

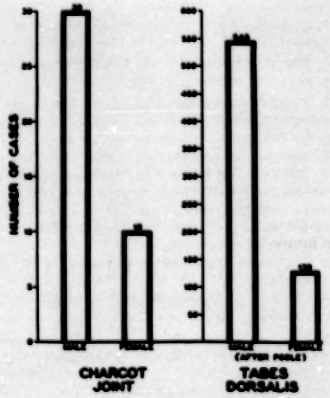



Fig. 2.—Sex incidence.

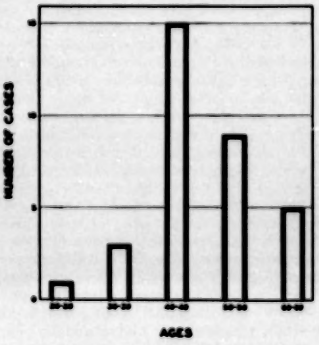



Fig. 3.—Age incidence: age of onset of Charcot joint.

From the Department of Surgery, Division of Orthopedic Surgery, University of California Medical School.
This material was demonstrated in space 522 in the Scientific Exhibit at the Eighty-Ninth Annual Session of the American Medical Association, San Francisco, June 13-17, 1938.

1. Charcot, J. M.: Lectures sur les maladies du système nerveux, 1868, New Sydenham Series: Sur quelques arthropathies qui paraissent dépendre d'une lésion du cerveau ou de la moelle épinière, Arch. de physiol. norm. et path. 1: 161, 1868.
2. Eloesser, Leo: On the Nature of Neuropathic Affections of the Joints, Ann. Surg. 66: 201 (Aug.) 1917.
3. Key, J. A.: Clinical Observations on Tabetic Arthropathies (Charcot Joints), Am. J. Syph. 16: 429 (Oct.) 1932.
4. Steindler, Arthur: The Tabetic Arthropathies, J. A. M. A. 96: 250 (Jan. 24) 1931.
5. Moritz, A. R.: Tabische Arthropathie, histologische Studie, Virchows Arch. f. path. Anat. 267: 746, 1928.
6. Wile, U. J., and Butler, M. G.: A Critical Survey of Charcot's Arthropathy: Analysis of Eighty-Eight Cases, J. A. M. A. 94: 1053 (April 5) 1930.
7. Knutsson, Folke: The Pathogenesis of Tabetic Skeletal Disease, Acta radiol. 18: 219, 1937.
8. Potts, W. J.: The Pathology of Charcot Joints, Ann. Surg. 86: 596 (Oct.) 1927.

In order to present graphically the clinical picture of a neuropathic joint, a series of forty cases of tabetic arthropathy was analyzed. The series includes the records of both private and clinic patients, about half of whom we ourselves observed. The diagnosis was well established in each case. A comparison of the sex incidence in this series with the observation, by Poole,[9] of the preponderance of male tabetic patients indicates an equal susceptibility of the two sexes to involvement of the joint, once the underlying disease is present (fig. 2). The average age at onset of symptoms in the joint appears to be between 45 and 50 years (fig. 3), the extremes being 29 and 68 years. The influence of trauma on the development of the arthropathy is seen in the ratio between the number of cases involving the lower extremities, fifty, and the number involving the upper extremities, seven (fig. 4). The importance of severe trauma in the initiation of the series of changes leading to a Charcot joint is further indicated by the history of the onset of symptoms immediately following an acute injury in eighteen cases, or almost half of the total number. The tendency to bilateral involvement is seen in sixteen cases in which two or more joints were affected. In this group both knees were involved in seven cases, both hips in four cases, both ankles in one

Fig. 4.—Joint involvement.

case and both wrists in another case. This occurrence of multiple Charcot joints in 40 per cent of our entire series, as compared with the usually accepted incidence of arthropathy in tabes dorsalis (6 per cent in a group of 744 cases of tabes cited by Moore [10]), suggests that certain victims of tabes have a predisposition to involvement of the joints. The importance of the careful observation of the pupillary and deep reflexes is shown by their almost universal impairment in the cases in our series (fig. 7), in contrast to the unreliability of the usual laboratory tests for neurosyphilis in the stage of the disease at which the arthropathy appears (fig. 8).

The microscopic changes which occur in the various components of a joint during the development of a neuro-arthropathy were described by Steindler [4] and by Moritz.[5] Studies of microscopic sections from eight Charcot joints in our series indicate that the primary pathologic process is a degeneration and partial disappearance of the articular cartilage which is invaded by fibrous connective tissue from the pannus on its surface (fig. 5). In certain areas the zone of preliminary calcification is exposed by the stripping away of cartilage. Beneath this zone there may be a proliferation of cartilage which becomes converted into subchondral bone, thus accounting for the sclerotic eburnated bone seen at the base of large defects in the articular cartilage (fig. 6). A generalized atrophy of

Fig. 5.—Articular surface of head of femur; patient O. V., aged 56, with Charcot hip of eighteen months' duration. *P*, fibrous tissue pannus on surface of cartilage; *C*, hyaline cartilage; *D*, degenerating area of cartilage invaded by fibrous tissue; *Z*, zone of preliminary calcification; *B*, subchondral bone; *M*, marrow. Slightly reduced from a photomicrograph with a magnification of 40 diameters.

the trabeculae of the cancellous bone is often seen. In one instance we observed a perivascular infiltration of lymphocytes in the capsule of the knee joint, although such evidence of inflammatory reaction is rare.

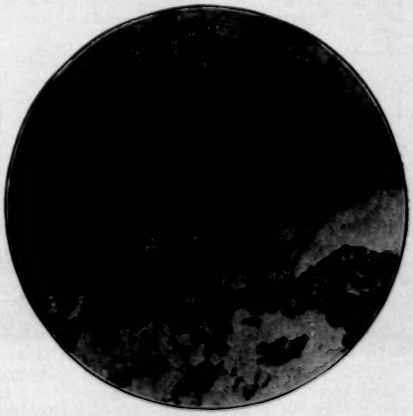


Fig. 6.—Articular surface of knee; patient K. S., aged 54, with Charcot knee of three years' duration. *C*, hyaline cartilage showing partial erosion; *B*, thickened subchondral bone forming under thinning cartilage; *Z*, zone of preliminary calcification; *M*, marrow. Slightly reduced from a photomicrograph with a magnification of 40 diameters.

In addition to the factors which lead to the disintegration of a joint, as shown in figure 1, we observed the presence of pyogenic organisms in an affected

9. Poole, A. K., cited by Weinberg, E. D.: The Treatment of Charcot Joints, South. M. J. 22:527 (June) 1930.
10. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, 1933, p. 394.

joint, as previously reported by Shands.[11] This author, in studying the synovial fluid from ten Charcot joints, found streptococci in two knees and Staphylococcus aureus in one shoulder. In our series of six joints on which operations were performed, culture of material obtained at operation from one knee yielded a mixture of hemolytic streptococcus and Staphylococcus aureus. In this case the operative wound suppurated and the joint failed to fuse. This experience indicates the importance of obtaining a bacteriologic study of the synovial fluid before operating on a Charcot joint.

### SUMMARY AND CONCLUSIONS

1. The diagnosis of a neuro-arthropathy rests on the observation of a swollen, relaxed and disorganized joint which is comparatively painless, in a case presenting the clinical signs of tabes dorsalis, syringomyelia or other involvement of the spinal cord.

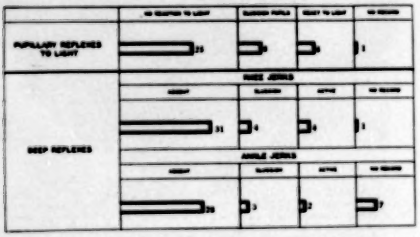



Fig. 7.—Reflexes of tabetic arthropathies.

2. A series of forty cases presenting sixty-five tabetic arthropathies was tabulated according to sex incidence, the age at which symptoms in the joint began, the occurrence of acute trauma as an initiating factor, the distribution of involvement of the joints, and the serologic and reflex features.

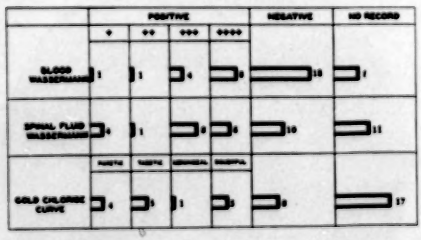



Fig. 8.—Serologic reaction of tabetic arthropathies.

3. The positive clinical evidence of rigid pupils and absent knee jerks is of much greater importance in the diagnosis of a tabetic arthropathy than are the various tests which are performed on the blood and spinal fluid.

4. A culture of the synovial fluid should be made prior to any operative procedure on a Charcot joint.

350 Post Street.

11. Shands, A. R., Jr.: Synovial Fluid in Infectious and Neuropathic Arthritis, South. M. J. **23**:818 (Sept.) 1930.

# KERATOSIS BLENNORRHAGICA

## A BRIEF REVIEW AND REPORT ON THE EFFECTS OF HYPERPYREXIA IN ITS TREATMENT

FRANK C. COMBES, M.D.
NEW YORK
CARLISLE DIETRICH, M.D.
TACOMA, WASH.
AND
JULIUS COHEN, M.D.
NEW YORK

In 1893 Vidal [1] described a generalized symmetrical eruption involving the nails in a patient with gonorrheal polyarthritis. In 1912 Simpson [2] described the first case occurring in the United States. Keim [3] in 1924 observed and recorded a similar case in which he made minute microscopic studies and reviewed all the pertinent literature, analyzing the disease from an etiologic angle and differentiating it from pustular psoriasis. Since 1924 there have been numerous additions to our knowledge of this syndrome, particularly concerning its response to treatment. Our purpose is to review briefly the more recent literature and to record studies made on two patients who have been under our care at Bellevue Hospital.

### ETIOLOGY

The genesis of keratosis blennorrhagica has been discussed by Génner and Boas,[4] Scomazzoni,[5] Rostenberg and Silver [6] and Ormsby in the discussion of a paper by Ebert and Slepyan,[7] the consensus being that the cutaneous reaction is an allergic expression of a sensitized skin, similar to the conception of the tuberculid reaction. Chauffard and Fiessinger [8] interpret the lesions as a manifestation of gonococcic septicemia in the presence of a severe arthropathy, although the finding of the gonococcus in the lesions has been infrequent. Barrett,[9] Wadsack,[10] Campbell,[11] DuBois,[12] Hansteen,[13] Scholtz [14] and Gager [15] report the isolation of a gram-negative diplococcus, but most attempts have been unsuccessful.

Results of efforts to induce lesions artificially by autoinoculation have been inconsistent. Lees and Percival [16]

From the Department of Dermatology, New York University College of Medicine, and the Dermatological Service of the Third (New York University) Medical Division, Bellevue Hospital, service of Dr. Edward R. Maloney.

1. Vidal, E.: Eruption generalisée et symétrique de croûtes cornées avec chute des ongles d'origine blennorrhagique, coincidant avec une polyarthrite de même nature: Récidive à la suite d'une nouvelle blennorrhagie deux ans après la guérison de la première maladie, Ann. de dermat. et syph. **4**:1 (1893).
2. Simpson, F. E.: Kératodermie blennorrhagique, J. A. M. A. **59**:637 (Aug. 24) 1912.
3. Keim, H. L.: The Histogenesis of Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **9**:423 (April) 1924.
4. Génner, Vigo, and Boas, Harald: Case of Gonorrheal Hyperkeratosis Without Gonorrhea, Hospitalstid. **73**:395 (March 27) 1930; Urol. & Cutan. Rev. **34**:365 (June) 1930.
5. Scomazzoni, T.: Considerazioni sulla patogenesi della cheratodermia blennorrhagica, Gior. ital. di dermat. e sif. **72**:716 (June) 1931.
6. Rostenberg, Adolph, and Silver, Henry: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **16**:741 (Dec.) 1927.
7. Ebert, M. H., and Slepyan, A. H.: A Case for Diagnosis (Keratosis Blennorrhagica?), Arch. Dermat. & Syph. **37**:106 (Jan.) 1938.
8. Chauffard, A., and Fiessinger, N.: Deux cas de kératose blennorrhagique: Reproduction expérimentale de la lésion cutanée, Bull. Soc. franç. de dermat. et syph. **20**:162, 1909.
9. Barrett, C. C.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **22**:627 (Oct.) 1930.
10. Wadsack, E.: Ein gonorrhoisches Exanthem, Berl. klin. Wchnschr. **43**:966, 1906.
11. Campbell, J. R., cited by Sutton, R. L.: Diseases of the Skin, ed. 5, St. Louis, C. V. Mosby Company, 1923, p. 438.
12. DuBois, C.: Keratoses blennorrhagiques ou dermatitis gonococciques, Acta dermat.-venereol. **5**:1, 1924; cited by Gans.[16]
13. Hansteen, E. H.: Keratosis Gonorrheica, Internat. Clin. **4**:162 (Dec.) 1927.
14. Scholtz, Moses: A Syndrome of Blennorrhagic Keratoderma, Arch. Dermat. & Syph. **15**:165 (Feb.) 1927.
15. Gager, E. C.: Keratodermia Blennorrhagica, J. A. M. A. **78**:941 (April 1) 1922.
16. Lees, David, and Percival, G. H.: Keratoderma Blennorrhagicum, Lancet **2**:1116 (Nov. 21) 1931.

obtained positive results by scarification, using pus obtained from the urethra. They were able also to produce similar lesions using cultures of gonococci. Sullivan, Rolnick and White [17] produced lesions by inoculation of scarified areas with scrapings taken from the exposed base of a lesion. However, Haase [18] maintains that any abrasion of the skin during the height of the eruption will result in the formation of a keratosis.

## INCIDENCE

This type of cutaneous lesion occurs in ratios ranging from 1:5,000 (Harrison [19]) to 1:7,500 (Brown [20]) cases of gonorrheal urethritis. It occurs almost exclusively in men during the third and fourth decades. Arning and Meyer-Delius,[21] who have had opportunity to study a large number of cases, report its frequency as about 0.46 per cent in 4,300 cases of gonorrheal urethritis. Isaac,[22] Lees,[23] Wayson,[24] Robert,[25] Lévy-Franckel,[26] Finlay,[27] Beatty [28] and Goldmann [29] have reported cases observed in women, but in some of them doubt was expressed by the author as to the accuracy of the diagnosis of a coexisting gonorrhea.

The disease is rare; Keim [5] in 1924 was able to find only fifty-eight cases in the literature. In 1933 Chambers and Koetter [30] listed sixteen additional cases including one of their own. Since then we have found nineteen case reports, making a total of ninety-three.

## CLINICAL COURSE

The onset of keratosis blennorrhagica is insidious and follows chronic and recurrent attacks of gonorrheal urethritis associated with chronic prostatitis and seminal vesiculitis. Chills and fever of a septic type herald the appearance of each crop of new lesions. In extensive cases there is profound prostration, anorexia and great loss of weight. The distribution of the eruption is symmetrical. There is a predilection for the soles and palms, genitals and groins. Less often the scalp, dorsum of the hands and feet, forearms and legs are involved. Lesions may also be found on the trunk, but this region and the face are not frequently affected. Barrett,[9] Berman,[31] Sherman, Blumenthal and Heidenreich,[32] Génner and Boas [4] and Chambers and Koetter [30] report lesions seen on the mucosa of the cheeks, tongue and hard palate.

As long ago as 1899 Buschke [33] recognized a variety of cutaneous lesions occurring in patients suffering from gonorrheal urethritis. He classified these as (1) simple erythema, (2) urticaria, (3) erythema nodosum, (4) hemorrhagic and bullous exanthems and (5) keratoses. Twelve years later [34] he modified this conception, recognizing only the keratoses, interpreting the other lesions merely as evolutionary, in which the dermal inflammatory process had been insufficient in duration or intensity to produce the typical crusts and scales.

*Lesions of Palms and Soles.*—Briefly stated, the pathologic process consists of vesiculation, pustulation and crusting with associated keratosis. The lesion at its inception consists of an erythematous macule. Hodara [35] recognized an urticarial wheal as the earliest manifestation in some cases. Nevertheless this type of

Fig. 1 (case 2).—Keratoses on dorsum of feet.

lesion is short lived, developing into a tiny vesicle surrounded by an erythematous halo. The lesion varies in size from pinhead to about a centimeter in diameter. It arises deep in the epidermis, since it contains an exceptionally small amount of cloudy fluid and may be called a dry vesicle, similar to those so frequently seen in dermatophytids and microbids. In a short time the lesion becomes waxy and almost translucent, like a pustule, although on incision it is perfectly dry. In the center a yellow spot appears, giving it an umbilicated appearance; but on palpation it is found to be a horny excrescence. Sometimes there is a peripherally attached scale suggesting the collaret of Biett seen in early papules of syphilis in the same location. Often there is definite grouping and confluence of individual papules to form circinate and serpiginous patches with

17. Sullivan, S. J.; Rolnick, H. C., and White, C. J.: Gonorrheal Keratosis: Case Report with Experimental Studies, Illinois M. J. **59**: 45 (Jan.) 1931.
18. Haase, M.: Keratosis Blennorrhagica; with Report of a Case, J. Cutan. Dis. **34**: 817 (Dec.) 1916.
19. Harrison, L. W.: Venereal Disease in General Practice, London, Oxford University Press, 1918.
20. Brown, W., and Hargreaves, H.: A Case of Gonorrheal Keratosis, Brit. J. Dermat. **29**: 107 (April-June) 1917.
21. Arning, E., and Meyer-Delius, H.: Beitrag zur Klinik der gonorrhoischen Hyperkeratosen, Arch. f. Dermat. u. Syph. **108**: 13, 1911.
22. Isaac, C. L.: A Case of Keratodermia Blennorrhagica in a Woman, Brit. J. Dermat. **32**: 195 (June) 1920.
23. Lees, D.: Keratodermia Blennorrhagica, Edinburgh M. J. **28**: 99 (March) 1922.
24. Wayson, J. T.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **24**: 291 (Sept.) 1931.
25. Robert, Emile: Contribution à l'étude des troubles trophiques cutanées dans la blennorrhagie, Thesis 360, Paris, 1897.
26. Lévy-Franckel, A.: Keratodermie Blennorrhagique, Ann. d. mal. vén. **13**: 385, 1918.
27. Finlay, D. K.: Keratodermia Blennorrhagica, Brit. M. J. **1**: 979 (June 6) 1931.
28. Beatty, J.: Symmetrical Hyperkeratosis of Extremities (Keratodermia Blennorrhagica), Brit. M. J. **1**: 14 (Jan. 1) 1927.
29. Goldmann, B. A.: Keratodermia Blennorrhagica: Report of Cases, Pennsylvania M. J. **37**: 299 (Jan.) 1934.
30. Chambers, S. O., and Koetter, G. F.: Keratosis Blennorrhagica, Arch. Dermat. & Syph. **27**: 411 (March) 1933.
31. Berman, L.: Ueber einen Fall von gonorrhoischer Keratose der Haut und Mundschleimhaut, Dermat. Ztschr. **51**: 420, 1928.
32. Sherman, W. L.; Blumenthal, F., and Heidenreich, J.: Blennorrhagic Balanitiform Keratoderma, Arch. Dermat. & Syph. **39**: 422 (March) 1939.
33. Buschke, Abraham: Exantheme bei Gonorrhoe, Arch. f. Dermat. u. Syph. **48**: 181, 1899.
34. Buschke, Abraham: Ueber universell symmetrische entzündliche Hyperkeratosen auf uro-septischer und arthritischer Basis, Arch. f. Dermat. u. Syph. **113**: 223, 1912.
35. Hodara: Ein Fall von Gondokokinie und generalisierten gonorrhoischen Exanthem, Dermat. Wchnschr. **55**: 397, 1912.

scaling borders and clearing centers. Half the sole may be entirely covered by one of these caked, heaped-up serosanguineous plaques. It requires approximately three weeks for the development of the mature lesion. Removal of the mass of dried blood, serum and scales exposes a very superficial dusky red, slightly moist, eroded surface with little or no bleeding. If the lesion is untreated, new crusts form. Healing leaves no scar, although Keim observed a slight degree of atrophy in the larger lesions resulting from healing below the rupial crust.

*Lesions of the Nails.*—Changes occurring in the nails do not differ clinically from those seen in favus and arthropathic psoriasis. There is a heaping up of yellow waxy material beneath the distal end of the nail plate. The nail itself becomes dry, brittle and opaque and is lifted from its base. The free border is rough, broken

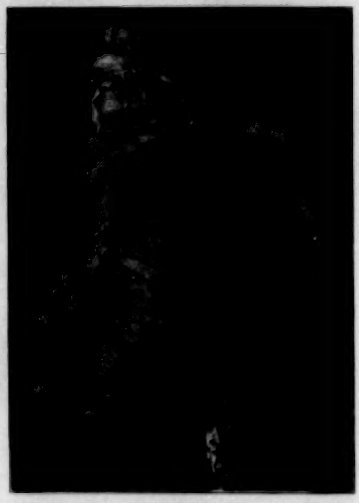


Fig. 2 (case 2).—Keratoderma of feet (a large keratosis on the left sole has been removed, exposing the base).

and jagged. These subungual keratomas are tender on pressure and may become painful. They may involve the nail independently or be continuous with keratoses of the adjacent integument of the fingers and toes, in which case there is an associated paronychia.

*Lesions of the Mouth.*—These consist of flat confluent grayish papules irregularly distributed over the hard palate, cheeks and borders of the tongue. They are usually not numerous and vary in size up to 0.5 cm. in diameter. At their inception they are minute red puncta which rapidly enlarge, so that within forty-eight hours they appear as umbilicated papules with an elevated grayish border. Their developmental cycle is much shorter than that of the cutaneous lesions; they disappear in a few days, leaving only dusky red eroded areas which heal without scarring.

*Lesions of the Joints.*—The arthropathy usually precedes the cutaneous lesions, although in rare instances it may be entirely absent. It differs from the usual gonorrheic monarthritis in the simultaneous involvement of a large number of articulations. The knee, ankle, wrist and acromioclavicular joints are those commonly affected. The pains are excruciating, but there is not as much redness and periarticular edema as one sees in rheumatoid arthritis or in monarthritic gonorrheal arthritis.

The progress of the disease is chronic with remissions and recurrences accompanied by fresh crops of lesions attending exacerbations of febrile and arthritic symptoms or induced by the therapeutic injection of gonococcus vaccine. Earlier writers expressed the opinion that the application of casts to the legs in the treatment of the arthritis was responsible for the cutaneous lesions.

Pathologic changes in many other organs have been noted by various investigators. These include endogenous conjunctivitis, corneal ulceration, iridocyclitis, anterior synechiae and retinitis. There is an associated general adenopathy in most cases. Acute glomerular nephritis has been reported by Spink and Keefer.[36] Other manifestations occurring less frequently include aortitis, pericarditis and endocarditis with large verrucous vegetations on the aortic valves. Tenosynovitis, bursitis and hepatitis with hypochromic anemia have been recorded also as occurring during the course of the disease.

## DIAGNOSIS

The recognition of keratosis blennorrhagica is not attended by any great difficulty when one considers the three essential requirements: the presence of gonorrhea, polyarthritis, and the characteristic cutaneous lesions. Jones[37] believes that the keratomas may constitute the only symptom other than the original gonorrheal urethritis.

Arthropathic psoriasis in former years offered some difficulty in differentiation. This is not unexpected, since the nail changes in the two conditions are similar and the cutaneous lesions of keratosis blennorrhagica and pustular psoriasis clinically and histologically resemble each other. Feldman[38] averred that he could see no difference between the clinical appearance of the two conditions. Silver[39] is of the opinion that keratosis blennorrhagica and psoriasis arthropathica constitute one syndrome with a variant etiologic factor. However, there are a few minor differences. Keratosis blennorrhagica at its inception is vesicular and shortly becomes pustular. Plasma cells are usually absent in arthropathic psoriasis. In arthropathic psoriasis there is a much greater tendency to ankylosis and deformity in the affected articulations. Furthermore, endogenous conjunctivitis never occurs in psoriasis.

Differentiation from syphilis may offer some difficulty. The superficial nature of the lesion should be sufficient to exclude the rupial syphilid. Some of the pustules look not unlike the early pustular eruptions but on palpation lack the shotty feeling. Acrodermatitis continua of Hallopeau must also be differentiated.

The search for gonococci in the skin has met with little success. Cole and Driver[40] found gram-negative intracellular diplococci in a smear from the base of a lesion on a patient's leg and from a miliary abscess on his scalp. The recovery of diplococci on blood culture

36. Spink, W. W., and Keefer, C. S.: Renal and Dermatologic Complications of Gonococcus Infections, New England M. Monthly **217**: 241 (Aug.) 1937.
37. Jones, T. R.: Unusual Case of Hyperkeratosis Blennorrhagica, Brit. M. J. **1**: 153 (Jan. 26) 1929.
38. Feldman, Samuel: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **27**: 889 (May) 1933.
39. Silver, Henry, in discussion on Feldman.[38]
40. Cole, H. N., and Driver, J. R.: Keratoderma Blennorrhagica, Arch. Dermat. & Syph. **19**: 1025 (June) 1929.

has been reported by Roark,[41] who questions the possibility of a contaminant. The demonstration of gonococci in blood smears by Hodara[35] is unique and has not been duplicated by other investigators. Although Löhe and Rosenfeld[42] attach great significance to the gonococcus fixation test, which they believe is regularly positive, as a rule it is of indefinite value and may be negative even with extensive involvement of both skin and viscera.

### HISTOLOGY

The histology has been completely discussed by Keim[3] and modified by Gans,[43] Simpson,[5] Haase[18] and Rostenberg and Silver.[6] Briefly, the fundamental changes are epidermal vesiculation with intracellular and intercellular edema. There is a subsequent leukocytic reaction, followed by pustulation with the rapid formation of a dry lamellar parakeratotic scale surmounted by a crust. This crust is often a prominent feature. Because of the predominance of the exudative process in some cases, Rostenberg considered the appellation "dermatitis rupioides arthropathica" a more appropriate name. Haase[18] considers parakeratosis the principal epithelial change. In the prickle cell layer there is a moderate degree of acanthosis with elongation of the rete pegs. In the papillary layer there are edema and an accompanying infiltration of lymphocytes, polymorphonuclear leukocytes, a few eosinophils and plasma cells.

### PROGNOSIS AND TREATMENT

The ultimate fate of patients afflicted with this syndrome is variable. An abortive type has been mentioned by Sherman, Blumenthal and Heidenreich,[44] designated as balanitis sicca circinata, in which the genitalia alone are involved. This type makes an early recovery. The severe generalized form may persist for many months or years, frequently resulting in death from septicemia or some intervening infection.

Modern treatment has improved the prognosis and favorably affected the duration of the disease. Local treatment is of little value. Ointments of resorcinol, salicylic acid and sulfur may be of benefit in their effect on the individual lesions. Autogenous vaccines have been found helpful by Scholtz.[14] Stock vaccines have not been of much value. Drainage of obscure foci in the prostate and seminal vesiculectomy, orthopedic care of the inflamed joints and general supportive management of the patient are indicated. Sherman, Blumenthal and Heidenreich[32] think that treatment of the primary focus is of most importance and that local treatment of the cutaneous and arthritic condition is of only secondary value. Infusions, transfusions and a high caloric diet with insulin and an adequate vitamin intake are helpful. Nonspecific protein therapy, copper, arsenic and ferruginous tonics should be given as necessary. Sulfanilamide and sulfarsphenamine have been administered but with indeterminate and inconsistent results. Willmott[45] had good results using a 1 per cent solution of mercurochrome intravenously.

The most effective therapeutic procedure is the induction of artificial fever by various means. It should constitute the nucleus around which all treatment is planned. Favorable response to this method has been reported by Willmott,[45] Cornbleet,[46] Epstein[47] and Epstein and Chambers.[48] Intravenous injections of typhoid-paratyphoid vaccine have not been attended by very consistent results. Epstein and Chambers report rapid improvement following the induction of a temperature in excess of 104 F. by the blanket method. All visible signs of the disease disappeared within a week and the arthritis greatly improved. Early cessation of fever therapy may be followed by a relapse if the primary focus of infection has not been eradicated. This method is valuable when patients are so toxic and debilitated that they cannot successfully withstand surgical intervention. In addition to improvement in the visible lesions and joints there is a rapid favorable response, both mental and physical, such as cannot be obtained by other means.

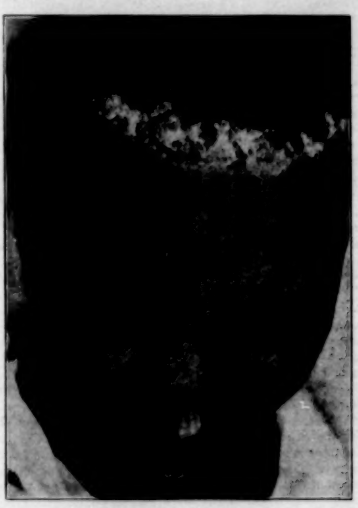


Fig. 3 (case 2).—Showing lesions of scalp.

### REPORT OF CASES

CASE 1.—*History.*—J. R., a white man, aged 22, was admitted to Bellevue Hospital in July 1937. His previous history was essentially irrelevant. He had gonorrheal urethritis of only four weeks' duration, for which he had had irrigations with a solution of potassium permanganate. Approximately two weeks before admission pain and swelling developed in both knees. Simultaneously there appeared crusted lesions on the soles and penis.

*Physical Examination.*—The patient had acute gonorrheal urethritis, prostatitis and arthritis involving both knee joints. The latter were red, swollen, tender and flexed at an angle of approximately 160 degrees. There was great limitation of motion, both active and passive, occasioned by the intense pain. The temperature was 102 F. and the pulse rate 100.

On the skin there were three groups of lesions, one on the soles, one on the penis and a third on the tongue. Those

41. Roark, B. H.: Blennorrhagic Keratosis, J. A. M. A. **89**: 2039 (Dec. 7) 1912.

42. Löhe, H., and Rosenfeld, H.: Klinische und physikalisch-chemische Untersuchungen über die Hyperkeratosenbildung bei Gonorrhöe und bei Psoriasis pustulosa arthropathica, Dermat. Ztschr. **59**: 355, 1929.

43. Gans, Oscar: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 348.

44. Blumenthal, F., and Sherman, W. L.: Penile Blennorrhagic Keratoderma with Abortive Course, Am. J. Syph., Gonor. & Ven. Dis. **22**: 176 (March) 1938. Sherman, Blumenthal and Heidenreich.[32]

45. Willmott, C. B.: "Kératodermie blennorrhagique" (Vidal), Arch. Dermat. & Syph. **13**: 17 (Jan.) 1926.

46. Cornbleet, Theodore, in discussion on Ebert and Slepyan.[7]

47. Epstein, Ervin: Hyperpyrexia in the Treatment of Keratoderma Blennorrhagicum, Am. J. Syph., Gonor. & Ven. Dis. **21**: 148 (March) 1937.

48. Epstein, Ervin, and Chambers, S. O.: Keratosis Blennorrhagica with Corneal Lesions, Arch. Dermat. & Syph. **36**: 1044 (Nov.) 1937.

on the soles were more or less confined to the anterior part and heel. They consisted of sharply defined, elevated dirty yellow conical keratomas with a dusky red erythematous halo. They varied in size and in one area had coalesced to form a coin sized patch. Some of the younger lesions were shiny and waxy, suggesting vesiculation. However, puncture of several of these lesions yielded no fluid. On the glans penis were three discrete crusted pea sized lesions. Grouped about the corona glandis and foreskin were several superficial irregularly shaped brownish erosions, the site of previous lesions. On the dorsum of the tongue were three pea sized painless well demarcated flat papules surrounded by a narrow zone of erythema. There was generalized adenopathy.

Dark field examination of the tongue and penile lesions was negative for Spirochaeta pallida. A urethral smear showed a few polymorphonuclear leukocytes with a sparse number of gram-negative intracellular diplococci. A blood culture showed no growth. A trichophytin intracutaneous test and a fixation test for gonorrhea were negative.

*Treatment.*—Ten cc. of azosulfamide was administered intramuscularly daily for sixteen doses with no improvement. Two days after the discontinuance of the medication the patient was placed in the inductotherm and the temperature of his body raised to 106 F. for a period of three and one-fourth hours. The following day his condition was greatly improved. The swelling in his knees had visibly receded and motion in the involved joints was very much increased. One week later the same treatment was administered for three hours. By this time the keratomas had entirely disappeared. Another treatment a week later of one and one-half hours' duration was followed by complete recovery.

CASE 2.—*History.*—C. G., a Negro, was admitted to Bellevue Hospital in January 1939. He had had several attacks of gonorrheal urethritis during the preceding three years. He had always been a heavy drinker. About the end of November some pain developed in the left ankle with associated redness and edema. Within a few days the left knee, right ankle, right knee and left shoulder were similarly affected, in that order.

*Examination.*—On admission he was moribund. His weight had decreased from 160 to 105 pounds (from 73 to 48 Kg.). There was extreme wasting of the muscles, especially of the thighs and legs. He suffered excruciating pains in both upper and lower extremities, with complete loss of active motion. All large joints of both extremities were red, swollen and tender. There were moderate limitation of motion and slight swelling and tenderness of the left shoulder joint. Both seminal vesicles were tender and distended, and the prostate was enlarged and boggy.

The cutaneous lesions were generalized but more profuse on the lower extremities. There were two distinct varieties, keratotic papules and irregularly shaped, well defined plaques. The former, which have been previously described in detail, were confined to his hands and feet. Some of them were situated beneath the free border of the nails, which were in some instances elevated from the nail bed and distorted. Irregularly distributed over the back of his feet, hands, legs, forearms, genitals, groins and abdomen were well defined keratotic plaques varying from 3 to 10 cm. in diameter. These were roughly conical and composed of laminated crusts, brownish yellow with a hard irregular surface. The frontal region of the scalp was more or less covered by an imbricated scale the layers of which were cemented together by a dried serosanguineous secretion. This extended beyond the margin of the hair onto the forehead. It was firmly adherent to the underlying skin and on removal left a smooth, superficial, dusky red, dry eroded surface.

Smears from the urethra were positive for gonococci. Examination of the blood on admission revealed erythrocytes 3,800,000, hemoglobin 75 per cent, leukocytes 7,600, polymorphonuclears 64 per cent, lymphocytes 32 per cent, mononuclears 4 per cent, antifibrolysin seven minutes, hemolytic streptococcus agglutination negative, hemolytic streptococcus precipitins (C) plus-minus, coagulation time four minutes, bleeding time seven minutes, Wassermann reaction negative, gonococcus fixation test negative, blood culture (ascitic fluid) negative, blood chlorides 429 mg., blood sugar 89 mg., blood nonprotein nitrogen 32 mg., icterus index 4, van den Bergh test negative.

*Treatment.*—For one week after admission sulfanilamide was administered in a dosage of 1 Gm. four times daily. In consideration of his profound prostration he was given pills of iron carbonate, viosterol, synthetic vitamin $B_1$, $B_2$ and nicotinic acid, 0.1 Gm. five times daily. In addition he received liver extract intramuscularly every other day and five blood transfusions. Under these procedures he rallied and showed considerable clinical improvement, although his erythrocyte count fell to 2,900,000 and his hemoglobin level to 50 per cent. The sulfanilamide had been discontinued but because of a recurrence of pain was resumed, with little benefit.

Beginning on March 3 and continuing at forty-eight hour intervals he received eleven treatments with the inductotherm. At each session his temperature was maintained at 104 F. for a period of from three to four hours. All lesions on his skin promptly disappeared and the arthritis rapidly subsided.

The improvement in his general physical and mental condition was even more striking. In five weeks he gained 40 pounds (18 Kg.) and his blood count returned to normal.

### CONCLUSIONS

1. Keratosis blennorrhagica is a distinct entity characterized by polyarthritis and cutaneous keratoses in the presence of a gonorrheal infection.

2. Fever therapy by means of the inductotherm offers a method of treatment superior to any which has been previously suggested.

80 West Fortieth Street.

---

## GALLSTONES IN CHILDREN

REPORT OF A CASE DIAGNOSED BY ROENTGEN EXAMINATION AND CONFIRMED AT OPERATION

VICTOR B. SEIDLER, M.D.
AND
ELIZABETH BRAKELEY, M.D.
MONTCLAIR, N. J.

Only a few years ago the occurrence of gallbladder disease in childhood was looked on as a pathologic curiosity. Not until Potter [1] in 1928 collected 224 cases from the literature, which he reviewed when reporting four cases from his own practice, did the medical profession begin to realize that many of the vague "stomach aches" of children were really manifestations of biliary disease. It is highly probable that this series of collected cases represented the merest fraction of the actual number of children afflicted with some disturbance of the biliary tract, for so firmly fixed was the idea that only adults are subject to gallbladder disease that the possibility was seldom or never considered. Many of the reported cases were accidental discoveries, found when operating for something else (usually acute appendicitis). Worse still, many were found at autopsy.

Ten years later, Potter [2] again took up the subject of gallbladder disease in childhood and, by instances from his own records and further explorations in the literature, was able to raise the total number of reported cases to 432. While admitting that this shows not so much a greater incidence of the condition in early life as more prompt recognition of a relatively common observation in pediatric practice, Potter is "firmly convinced that, at the present time, gallbladder surgery

1. Potter, A. H.: Gallbladder Disease in Young Subjects, Surg., Gynec. & Obst. **46**: 795 (June) 1928.
2. Potter, A. H.: Biliary Disease in Young Subjects, Surg., Gynec. & Obst. **66**: 604 (March) 1938.

in children is several years in arrears of the symptoms. This is emphasized by the fact that a large majority of cases of gallbladder disease in the third and fourth decades give histories of symptoms dating back to the first or second decade."

Our attention was first drawn to the subject of gallbladder disease in childhood by a patient admitted to the Mountainside Hospital, through the pediatric clinic. Reviewing the literature, it is astonishing to find how many cases are on record, yet how seldom the diagnosis is made in the regular routine of hospital admission. Besides Potter's two papers, which cover aspects of the subject completely, there are a number of other isolated case reports of cholelithiasis in children in the literature.[3]

## ETIOLOGY

When biliary disease manifests itself in infants, one naturally thinks of congenital obstruction as a probable etiologic factor. This aspect of the subject has been well presented by Ladd, who studied forty-five cases at the Children's Hospital, Boston. The biliary system, like other parts of the digestive and excretory tract, is subject to various congenital anomalies, several of which may cause obstruction to the ducts. There may be atresia of the hepatic ducts or of the common duct, and the extrahepatic ducts may be missing entirely. The gallbladder may be merely represented by a small cyst having no connection with the common duct or, again, there may be no common or hepatic ducts. There may be stenosis of the common duct and complete obstruction may take place because it is easily plugged with inspissated bile. Or partial obstruction may be due to congenital narrowing of the common duct. Very serious malformations are likely to be manifested by deep jaundice or other clinical evidences before the infant attains many weeks of age. The majority do not survive, although a few have been completely relieved by operation.

Such a relatively unimportant deformity as congenital narrowing of a duct may, however, give no decided evidence of its presence until the child attains some age, yet the damage to the biliary system is steadily progressing and the symptoms which it continually gives are ignored or misinterpreted. Common duct obstruction has been successfully relieved by anastomosis of the gallbladder to the duodenum (cholecystoduodenostomy), but it is evident that only surgical treatment will enable these patients to outlive infancy.

In older children the etiologic factor in gallbladder disease is more likely to be an acute infection—one of the exanthems, influenza or typhoid fever. Typhoid was formerly incriminated in all types of gallbladder disease, but improvements in sanitary precautions have reduced the incidence of this infection almost to the vanishing point in many communities, yet the number of cases of biliary disease shows no decrease. Scarlet

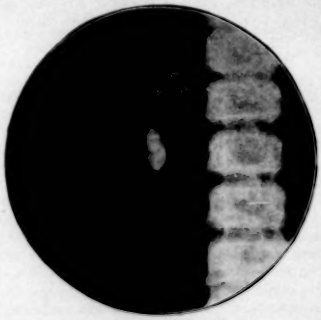


Fig. 1.—Appearance of gallbladder.

fever is still prevalent enough to account for many instances, and infections of the upper respiratory tract, with influenza, contribute many more. In Lowenburg and Mitchell's series, five children had an associated infection of the respiratory tract. Focal infection and metastasis from a chronically diseased appendix are likewise cited by some writers as prominent etiologic factors in the cholecystitis of childhood. Mention should also be made of the possibility of Lamblia infection; as far back as 1928 Smithies found this parasite when doing biliary drainage, and its pathogenicity, when lodged in the biliary tract, has since been recognized by numbers of surgeons operating on the gallbladder and ducts. Twelve of the young patients of Zelditch and his co-workers harbored the parasite, which was recovered in the returns from biliary drainage.

## SYMPTOMS AND DIAGNOSIS

In making the diagnosis of gallbladder disease, the physician's task is somewhat complicated if the patient is a child. This is because even at the present time comparatively little is said or written about the prevalence of biliary tract disease in children. Even when a child's complaints are promptly heeded and not placated with some home remedy for a "stomach ache," the possibility of gallbladder disease will not be considered. It is noticeable that many of the cases of

3. These include:
Wendel, A. V.: A Contribution to the Symptomatology and Diagnosis of Cholelithiasis in Infancy and Childhood, M. Rec. **54**: 41, 1898.
Kellogg, E. L.: Gallbladder Disease in Childhood, Ann. Surg. **77**: 587 (May) 1923.
Zambalos, Andreas: Nephrolithiasis und Cholelithiasis im Jugendalter, Röntgenpraxis **9**: 416 (June) 1937.
Berman, J. K.: Acute Cholecystitis with a Gallstone in a Child Eleven Years of Age, J. Pediat. **5**: 47 (July) 1934.
Hamilton, H. B.; Rich, C. O., and Bisgard, J. D.: Cholecystitis and Cholelithiasis of Childhood, J. A. M. A. **103**: 829 (Sept. 15) 1934.
Skemp, A. A.: Gallstones in Infancy, ibid. **90**: 108 (Jan. 10) 1931.
Montgomery, A. H.: Diseases of the Gallbladder in Children, Am. J. Dis. Child. **44**: 372 (Aug.) 1932.
Judd, E. S.: Certain Differences Presented by Diseases of the Biliary Tract, S. Clin. North America **5**: 643 (June) 1925.
Brown, W. S.: Cholelithiasis in a Child of 3 Years and 8 Months, M. J. Australia **2**: 53 (July 13) 1935.
Farr, C. E.: Cholecystitis and Cholelithiasis in Children, Arch. Pediat. **39**: 574 (Sept.) 1922.
Eisendrath, D. N.: Gallstones in Infancy and Childhood, Ann. Surg. **66**: 557 (Nov.) 1917.
Reid, M. R., and Montgomery, J. C.: Acute Cholecystitis in Children as a Complication of Typhoid Fever, Bull. Johns Hopkins Hosp. **31**: 7 (Jan.) 1920.
Snyder, C. C.: Cholecystitis and Cholelithiasis in Young Children, J. A. M. A. **85**: 31 (July 4) 1925.
Zelditch, Wurmann, Jedkver and Guinditch: Des cholécystites chez les enfants, Rev. franç. de pédiat. **12**: 331, 1936.
Smithies, Frank: Present-Day Treatment of Intestinal Protozoiasis, J. A. M. A. **91**: 152 (July 21) 1928.
Vergelin, M. E., and Rosenfeld, Adolf: Tuberculosis pulmonary litiasis biliar concomitantes en una niña de seis años de edad, Semana méd. **1**: 1307 (June 9) 1938.
Ladd, W. E.: Congenital Obstructions of the Bile Ducts, Ann. Surg. **102**: 742 (Oct.) 1935.
Lowenburg, Harry, Jr., and Mitchell, A. G.: Cholecystitis in Childhood, J. Pediat. **12**: 203 (Feb.) 1938.
Guilleminet; Pouzet, P., and Truchet: Biliary Lithiasis in a Child, Lyon méd. **158**: 429 (Oct. 18) 1936.
Beals, J. A.: Cholecystitis and Cholelithiasis in Children, South. M. J. **21**: 666 (Aug.) 1928.
McClendon, S. J.: Gallstones in Children: Case Diagnosed by Roentgen Examination, Am. J. Dis. Child. **45**: 584 (March) 1933.
Sadel, I. P.: Cholecystitis and Cholelithiasis in Childhood, Arch. Pediat. **55**: 669 (Nov.) 1938.
Amberg, Samuel, and Walters, Waltman: Infantile Jaundice; Report of Two Unusual Cases in Which Cholecystotomy Was Employed, Proc. Staff Meet., Mayo Clin. **12**: 769 (Dec. 7) 1938.
Penberthy, G. C., and Benson, C. D.: Surgery of the Biliary Tract in Infants and Children, Am. J. Surg. **40**: 232 (April) 1938.
Swing, A. T., and Bullowa, J. G. M.: Acute Cholecystitis Complicating Typhoid Fever, Am. J. Dis. Child. **55**: 521 (March) 1938.
Doane, V. J.: Acute Cholecystitis Occurring in an Infant, Brit. J. Surg. **25**: 914 (April) 1938.

childhood cholecystitis were discovered only when the abdomen had been opened to extirpate a supposedly inflamed appendix. Unlike our patient, the majority of these little patients are brought not to pediatricians but to general surgeons, on whom the task of recognizing the true nature of the abdominal condition usually devolves.

Fig. 2.—Appearance at operation.

The chief diagnostic method is roentgenography. Only three cases have been reported in which the diagnosis was first made by x-rays and later confirmed by operation: one by Beals, one by Montgomery and one by McClendon. Cholecystography is usually well tolerated by children and should be regularly employed with all obscure abdominal conditions, particularly if the child shows even slight jaundice. The routine use of this diagnostic aid would undoubtedly uncover many more cases of gallbladder disease in the early years of life and in this way contribute to better health among the adult population.

The symptoms displayed by children suffering from cholecystitis or cholelithiasis are so similar to those due to appendicitis that confusion between the two is very common. Moreover, it is not unusual for the two conditions to exist simultaneously. Therefore, when operating for appendicitis in a young patient, investigation of the condition of the biliary canal should not be omitted even when the appendical features are quite sufficient for all the symptoms.

Several authors have recently stressed the importance of examination of the bile and duodenal intubation in the establishment of a diagnosis of gallbladder disturbance, either suspected or positively recognized. Flakes of mucus, often loaded with leukocytes, were seen by Zelditch and his assistants, and when there was a tendency toward cholelithiasis, cholesterol was demonstrated in the bile.

## TREATMENT

In all cases surgical therapy is the only means of relief. Some of the earlier writers on gallbladder ailments in childhood tended to stress the medical side of the picture. But most of those who have recently made contributions to the literature on this subject condemn any undue delay in undertaking surgical exploration.

## REPORT OF CASE

*History.*—A 10 year old Negro girl was first seen in the pediatric clinic with the chief complaint of loss of appetite and weakness, accompanied by jaundice, light colored stools and dark urine of two weeks' duration.

The history, given by the child's mother, was of recurrent attacks of jaundice since the age of 4, sometimes with intervals of no longer than four months. Associated with the jaundice was pain, felt across the middle of the back and on both sides. But there never had been abdominal pain typical of gallstone colic. There had been rheumatic fever at 4 years and, following this, feverish intervals when the child complained of pain in her knees. There had been frequent attacks of otitis media. At about 8 years of age she had been sent to Glen Gardner Tuberculosis Sanatorium with a diagnosis of pulmonary tuberculosis, where she remained thirteen months and was then discharged as having the disease in arrested condition. She was said to have suffered several attacks of jaundice while in the sanatorium, but apparently no investigation of its cause was ever attempted.

*Physical Examination.*—The patient was well developed and well nourished but looked chronically ill. The conjunctivas were markedly jaundiced. There was a perforation of the right ear drum. The tonsils had been incompletely removed so that some small tags were still in evidence in a throat which was slightly injected. The lungs were clear to percussion and auscultation. The heart was slightly enlarged to the left and there was a loud systolic murmur best heard at the apex and transmitted to the axilla. The liver and spleen were not palpable, and the only positive abdominal indication was slight tenderness on deep pressure in the right upper quadrant.

The patient was admitted to the pediatric ward for complete investigation. The table gives the results of laboratory examinations.

*Roentgen Examination.*—The plain x-ray film showed a large number of small calcareous stones, mostly in the gallbladder, although four or five were in the cystic and hepatic ducts. Results of study by the Graham dye method were identical.

*Laboratory Data*

| Test | Result |
|---|---|
| Icteric index | 25 |
| Van den Bergh (both direct and indirect) | Negative |
| Blood phosphorus | 4.7 mg. |
| Blood phosphatase | 14 units |
| Blood cholesterol | 176 units |
| Stool examination: | |
| Urobilin | present |
| Bilirubin | absent |
| Blood count: | |
| Hemoglobin | 55% |
| Red blood cells | 3,130,000 |
| White blood cells | 12,900 |
| Polymorphonuclears | 56% |
| Small lymphocytes | 44% |

*Operation.*—Because of the low blood count, it was deemed unwise to operate immediately. Two blood transfusions were given and at the end of two weeks the blood had improved sufficiently to permit surgical intervention. On April 8, 1939, under gas-oxygen-ether anesthesia, the abdomen was opened by an incision extending from the costal margin to the level of the umbilicus, 1 cm. to the right of the midline. The gallbladder, when exposed, was found to be greatly enlarged and filled with small stones. One stone was found in the ampulla and another at the junction of the cystic and common ducts. The gallbladder was freed and dissected from the liver, the cystic artery identified, clamped, tied and cut; the common duct

Fig. 3.—The operative specimen.

was dilated with Lahey dilators as far as the duodenum and the gallbladder was then removed. The wound was closed in the usual manner.

A feature of much interest was a group of glands about the common duct which were enlarged and very firm. One of these glands lay in such a position that it pressed on the common duct, almost completely occluding its lumen. The stone already mentioned lay directly behind the point of compression. The gland was removed and sent to the laboratory for examination.

*Pathologic Report.*—The gallbladder was thickened and infiltrated with fibrous connective tissue. There were dilated capillaries and focal collections of chronic inflammatory cells. The gland which had been removed showed no tuberculous infection.

*Postoperative Course.*—At her discharge from the hospital, after an uneventful convalescence, the child's icteric index was 11.

### COMMENT

The striking feature of this case is the finding of nontuberculous glands in close relation to the diseased gallbladder. The history of arrested pulmonary tuberculosis would at once suggest their origin, but the laboratory examination did not bear this out. The fact that a stone had formed directly behind the point of compression of the common duct strongly indicates the important role of stasis of bile in the formation of stones.

Examination of the case reports of gallbladder disease in children brought to light two which bear some resemblance to that just related. Patient 4 of Zelditch and his co-workers was sent to the hospital with a diagnosis of tuberculous peritonitis. There had been abdominal pain for more than a month, but no details of a tuberculous history are given. The child was treated with biliary drainage only. Vergelin and Rosenfeldt's patient was a girl of 6 years who had active pulmonary tuberculosis at the time the gallbladder symptoms were first manifest. At operation a number of the mesenteric glands were noted as enlarged and palpable as hard nodules along the course of the ducts. No mention is made of these enlarged glands exerting pressure on any of the ducts, but this would seem to be a logical result of caseation of the mesenteric glands, if one accepts the theory of the bile stasis origin of gallstones.

### CONCLUSIONS

As nearly 450 cases of gallbladder disease in children under 15 years of age are now on record, disorders of the biliary tract in children can no longer be regarded as rare.

2. Typhoid, once regarded as a common cause of cholecystitis, has now become an unimportant source of morbidity, thanks to prophylaxis and improved sanitation. But the incidence of cholecystitis and cholelithiasis in children has in no wise diminished, so one must look elsewhere for the chief etiologic factors.

3. From the observations at operation in the case here reported, it is probable that bile stasis, induced by compression of the common duct by an enlarged and indurated node, was the basic cause of the cholelithiasis.

4. The diagnosis of biliary tract disease during the early years of life may be reached by the same methods now employed for adults and is in no way more complicated or difficult than with adults. Because the symptoms so closely simulate those of appendicitis, differential diagnosis is often missed. Therefore the pediatrician and the surgeon should be on the alert to recognize gallbladder disease unerringly and to operate promptly when surgical treatment is indicated.

16 Plymouth Street—71 Myrtle Avenue.

## EXPERIENCES IN HEPARIN ADMINISTRATION

ROY D. McCLURE, M.D.
AND
CONRAD R. LAM, M.D.
DETROIT

The control of the coagulability of the blood in vivo by the use of heparin in its present highly purified form constitutes one of the significant achievements of medical science during the past decade. The product available today is 500 times more potent than the original crude heparin described by Howell and Holt[1] in 1918 and is 100 times more potent than the material used clinically by Mason[2] in the Henry Ford Hospital in 1924. In that year Mason reported the experience with heparin as the anticoagulant in blood transfusions in thirty-three human subjects. He used 100 mg. of heparin in 500 cc. of blood. Reactions were frequent, the incidence for three lots being 33 per cent, 100 per cent and 28 per cent respectively. About one-half hour after the transfusions, symptoms developed which varied in intensity from mild headache and chilly sensations to intense headache, backache, vomiting, chills and temperatures as high as 104.4 F.

In animal experiments, Mason[3] noted that heparin was efficacious in preventing experimental thrombosis and suggested that it should be applicable clinically. No attempt was made at the general heparinization of a human subject because of the untoward reactions resulting from the injection of enough heparin to render only half a liter of blood incoagulable.

In 1929 Howell[4] reported that he had purified the material so much that 1 mg. would prevent the clotting of 100 cc. of blood. It had been used in ten transfusions with two chills resulting. The problem of further purification was undertaken by workers in Toronto in 1929. At the suggestion of Dr. C. H. Best, Charles and Scott,[5] of the Connaught Laboratories of the University of Toronto, did successful research on heparin and produced the present highly purified nontoxic material which we are using. A number of investigators have done valuable independent research on the subject. For a summary of the contributions of Schmitz and Fischer, Jorpes and Bergstrom, Astrup and Jensen and other workers, the reader is referred to the recent comprehensive review by Mason.[6]

After animal experimentation, Murray, Best and their co-workers used heparin on human subjects. Their experiences have been presented in a number of papers.[7] In Murray's latest paper he[8] summarizes his extensive

From the Division of General Surgery of the Henry Ford Hospital.

1. Howell, W. H., and Holt, E.: Two New Factors in Blood Coagulation—Heparin and Pro-Antithrombin, Am. J. Physiol. **47**: 328-341 (Dec.) 1918.

2. Mason, E. C.: A Note on the Use of Heparin Blood Transfusion, J. Lab. & Clin. Med. **10**: 203-206 (Dec.) 1924.

3. Mason, E. C.: Blood Coagulation: The Production and Prevention of Experimental Thrombosis and Pulmonary Embolism, Surg., Gynec. & Obst. **39**: 421-428 (Oct.) 1924.

4. Howell, W. H.: The Purification of Heparin and Its Chemical and Physiological Reactions, Bull. Johns Hopkins Hosp. **42**: 199-206 (April) 1928.

5. Charles, A. F., and Scott, D. A.: Studies on Heparin: IV. Observations on the Chemistry of Heparin, Biochem. J. **30**: 1927-1933 (Oct.) 1936.

6. Mason, M. F.: Heparin: A Review of Its History, Chemistry, Physiology and Clinical Applications, Surgery **5**: 451-467 (March), 618-637 (April) 1939.

7. Murray, D. W. G.; Jaques, L. B.; Perrett, T. S., and Best, C. H.: Heparin and the Thrombosis of Veins Following Injury, Surgery **2**: 163-187 (Aug.) 1937. Murray, D. W. G., and Best, C. H.: Heparin and Thrombosis: The Present Situation, J. A. M. A. **110**: 118-119 (Jan.) 1938; The Use of Heparin in Thrombosis, Ann. Surg. **108**: 163-177 (Aug.) 1938. Best, C. H.: Heparin and Thrombosis, Brit. M. J. **2**: 977-981 (Nov.) 1938.

8. Murray, D. W. G.: Heparin in Surgical Treatment of Blood Vessels, Arch. Surg. **40**: 307-325 (Feb.) 1940.

clinical experience with heparin. A group of 440 patients with various operative procedures had been given prophylactic heparinization, and no pulmonary embolism had occurred. Twenty-nine patients with pulmonary embolism had been treated; all of these survived, and with one possible exception there was no further embolism. Eighty-one patients with phlebitis were treated, and it was felt that the clinical course of the treated group was better than that of a control group; no emboli occurred. Six patients with mesenteric thrombosis were given heparin after operation to prevent extension of the process; four recovered and two died of preexisting peritonitis. Heparin was used in eight cases of splenectomy to prevent thrombosis of the portal vein. Embolectomy for peripheral embolism was done twelve times, the artery remaining patent in each instance; two end to end arterial sutures were done (brachial and common carotid arteries) and in one case a venous graft was used to bridge the gap in a popliteal artery left after the removal of an aneurysm. A secondary operation was necessary in the latter case but the result was excellent.

In a preliminay report Kelson and White[9] showed encouraging results in the treatment of seven patients who had bacterial endocarditis with a combination of sulfapyridine and heparin.

In the face of the impressive report of Murray, we present our results with heparin administration in a small series of eleven cases. We believe that these patients presented definite if not urgent indications for heparinization; the material was not used from the standpoint of research but was used for the treatment of the individual patients and was paid for by the patients as such. Even in this small series we have had a reasonable opportunity to study the potency of the material in vivo and its possible toxic effects. Several details of the technic of administration have been learned by experience, and a few complications have arisen which are worth recording.

Since April 1939, every patient with postoperative embolism which was not immediately fatal has received general heparinization as prophylaxis against further embolism. We have had eight such patients. Seven of these did not have recurrence of embolism; one had a second infarction five days after the first course of heparin was finished, and a second course was given, with recovery resulting. Three other types of condition have been treated: embolectomy for embolus in the popliteal artery, thrombosis of the posterior tibial artery, and phlebitis. The clinical data in the eleven cases are summarized in the accompanying table.

*Summary of Eleven Cases Treated with Heparin by Continuous Intravenous Drip*

| No. | Patient | Age | Sex | Weight | Operation or Diagnosis | Indication for Heparin | Evidence of Pulmonary Embolism | | | | Days of Heparin | Approximate Units per Hour Necessary | Total Number 10 Cc. Vials | Chills |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Typical History | Physical Signs | Hemoptysis | X-Ray Evidence | | | | |
| 1 | W. P. | 25 | ♂ | 191 | Hernia | Embolism | + | + | + | + | 6 | 2,000 | 20 | 3 |
| 2 | B. S. | 49 | ♀ | 157 | Hernia, phlebitis | Embolism | + | + | + | + | 15 | 1,000 | 40 | 4 |
| 3 | N. V. | 74 | ♂ | 154 | Fractures | Embolism | + | + | + | ? | 10 | 2,000 | 40 | 2 |
| 4 | S. K. | 37 | ♂ | 180 | Perforated appendix | Embolism | + | + | + | + | 9 | 2,000 | 40 | 1 |
| 5 | E. S. | 45 | ♀ | 161 | Ovarian cyst | Embolism | + | + | 0 | 0 | 5 | 1,000 | 11 | 1 |
| 6 | M. S. | 52 | ♂ | 132 | Hernia | Embolism | + | + | 0 | ? | 6 | 1,500 | 20 | 1 |
| 7 | G. L. | 62 | ♂ | 117 | Popliteal embolus | Embolectomy | — | — | — | — | 5 | 2,000 | 20 | 0 |
| 8 | A. R. | 45 | ♂ | 174 | Hernia | Embolism | + | ? | 0 | + | 9 | 1,000 | 17 | 0 |
| 9 | F. M. | 42 | ♂ | 210 | Peritonitis | Phlebitis | — | — | — | — | 6 | 2,000 | 18 | 0 |
| 10 | J. M. | 35 | ♂ | 152 | Tabetic dementia paralytica | Thrombosis of artery | — | — | — | — | 2 | 2,000 | 11 | 0 |
| 11 | W. K. | 69 | ♂ | 187 | Prostatectomy | Embolism | + | + | 0 | + | 8 | 2,000 | 28 | 0 |

The material consists of 10,000 units of heparin dissolved in 10 cc. of saline solution. (This unit is five times larger than the original Howell unit, which inhibits the clotting of 1 cc. of cat's blood.) We proceeded to give this material to our first patient (W. P., chart 1) according to the simple directions given by Murray and Best in January 1938.[7]

> The heparin solution is added to an intravenous saline drip. Usually 1,000 units of heparin, i. e. 10 mg., is added to each 100 cc. of saline solution. The saline and heparin mixture is allowed to run into the vein at such a rate that the clotting time of the patient's blood is maintained at about fifteen minutes, i. e. two or three times the normal value. . . . The rate of saline solution may be twenty-five drops per minute, but this varies greatly from case to case. . . . The clotting time may be determined by one of the simple methods, such as the breaking off of bits of a capillary tube which has been filled with blood.

Chart 1 shows graphically what we were able to do with the clotting time in the first case. Injection of the solution was begun at the rate of 2,000 units an hour. Two hours after the treatment was begun the patient had a violent chill. In spite of this reaction the treatment was continued. The temperature rose to 103 F. and on two subsequent days there were less severe chills. The rate of injection was varied in an attempt to stabilize the clotting time at the optimum level, and it will be seen that approximately 2,000 units an hour was necessary to elevate the clotting time to fifteen minutes or above. In contrast to this the results in our eighth case are shown in chart 2. The clotting time in this case was easily maintained above the optimum level by the administration of 1,000 units an hour. No chill or other subjective symptoms occurred in this case, indicating that the toxic fractions in the material used in our earlier cases had been removed.

Our third case (N. V., chart 3) is reported in detail because it illustrates a complication that may be expected if one attempts to maintain an optimum clotting time in all patients by giving 1,000 units in 100 cc. of saline solution. Since some patients require 2,000 units an hour, this would result in the administration of 4,800 cc. of saline solution daily. In the presence of healthy kidneys and heart this will be tolerated for a period, but after this edema appears.

A white man aged 24 was admitted July 13, 1939, suffering from fractures of eight ribs on the left side and both scapulas. July 30 he had a sharp pain in the right side of the chest

9. Kelson, S. R., and White, P. E.: A New Method of Treatment of Subacute Bacterial Endocarditis Using Sulfapyridine and Heparin in Combination: A Preliminary Report, J. A. M. A. 113:1700-1702 (Nov.) 1939.

posteriorly and coughed up blood; roentgenologic examination showed probable infarction. Heparinization was begun August 1; he immediately had a chill with rise of temperature to 104 F. August 2 he was comfortable; August 3 a slight expiratory wheeze was noted, and August 4 there was slight increase in respiratory difficulty. The next day generalized edema appeared and the patient was mentally confused. It was evident that these symptoms were due wholly to excessive parenteral intake of physiologic solution of sodium chloride. Therefore the concentration of heparin was doubled. August 6, studies of the blood chemistry showed the chlorides to be 430 mg. (whole blood as sodium chloride), sodium 338 mg., carbon dioxide combining power 77.6 volumes per cent, plasma albumin 2.68 Gm. and globulin 1.65 Gm. The alkalosis and the marked dilution of the blood as indicated by the low plasma proteins values were notable. The edema did not disappear rapidly, and August 7 a 5 per cent solution of dextrose was substituted for the saline solution. This resulted in marked diuresis and rapid disappearance of the edema. A mild saphenous phlebitis resulted from the use of dextrose as the infusion medium, but the patient had no further embolic manifestations and was discharged on September 2.

When a person with cardiac insufficiency is treated with heparin, the matter of the injection of saline solution into the blood stream is of the greatest importance. This may explain why it was necessary for Kelson and White to discontinue prematurely the treatment in four of their seven cases of endocarditis. Our seventh case

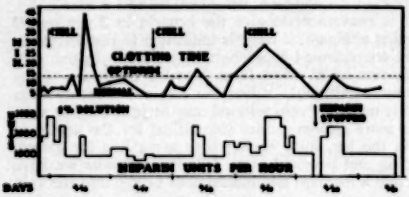



Chart 1 (W. P.; herniotomy; embolism ninth day).—Heparin chart of the first patient in the series, showing that 2,000 units an hour was necessary to maintain the clotting time at fifteen minutes or above (capillary tube method).

(G. L. in the table) illustrates a satisfactory result from peripheral embolectomy in spite of the fact that it was necessary to stop the heparin early because the patient would not tolerate the amount of saline solution necessary to give the heparin in a concentration of 4,000 units per hundred cubic centimeters.

A white man aged 62 had been treated for arteriosclerotic heart disease with auricular fibrillation since 1937. He had had seven admissions for congestive failure. Oct. 10, 1939, he was admitted on the service of Dr. F. J. Smith for treatment of myocardial failure. November 4 there was sudden loss of vision of the left eye, and ophthalmologic examination revealed central retinal thrombosis. At 8 a. m. November 6 he had sudden severe pain in the left popliteal space. Examination of the leg showed it to be blanched and cold below the knee. There was no pulse in the posterior tibial artery, but a faint pulse could be felt in the upper part of the popliteal artery. The pain was excruciating and was not controlled with morphine. The diagnosis of embolus to the bifurcation of the popliteal artery was made. General heparinization was begun at once, so that when the patient was brought to the operating room the clotting time was twice normal. Operation (R. D. McC.) was begun at 11 a. m. under general anesthesia. The popliteal artery was exposed and the embolus palpated and removed after incision of the artery. The sclerotic artery was sutured with arterial silk, and when the proximal serrefine clamp was removed there was immediate pulsation in the posterior tibial and dorsalis pedis arteries. Heparinization was maintained throughout the operation.

When the patient reacted from the anesthetic, his gratitude for the relief of the agonizing pain of ischemia was notable. It was planned to give heparin for a week, but on November 11, the fifth day, Cheyne-Stokes respirations and signs of increas-

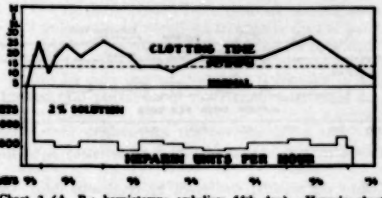



Chart 2 (A. R.; herniotomy; embolism fifth day).—Heparin chart of eighth patient in the series, whose clotting time was easily maintained at the optium level by giving 1,000 units an hour. Note the absence of chills.

ing myocardial failure developed, and it was deemed imperative to discontinue all intravenous fluids. There was slight oozing of the wound, which was easily controlled with pressure dressings. The circulation of the foot remained excellent. The patient had marked diuresis from a mercurial diuretic, a hydrothorax was tapped November 20, and he was discharged December 12.

Our eleventh case (W. K.) is reported in detail because of the complications encountered and the marked change in the method of administration of the second course of heparin:

A white man aged 69 had a suprapubic cystotomy Feb. 15, 1940, and on February 26 the second stage of the prostatectomy was done. Three days later there developed pain and a friction rub in the left chest. Injection of heparin in 2 per cent solution was begun. On March 3 auricular fibrillation was noted, and it was felt that some degree of cardiac decompensation existed. He was digitalized, and the heparin was continued in 4 per cent solution. On March 8 he was drowsy and there was slight pitting edema of the sacrum and left ankle. It was felt advisable to discontinue the heparin and allow the patient to get up. Activity had progressed to the point where he was walking in the hall on March 13. That night sudden pain developed in the right axilla. It was evident that a second infarction had occurred, but the cardiorespiratory consultant advised against the administration of any considerable quantity of fluids intravenously on account of the previous experience. On March 14 there was a loud leathery friction rub over the right axilla. On March 15 it was decided to try the intermittent injection of the undiluted heparin solution. A previous report[10] had shown that three injections over a period of six hours gave a maximum elevation of clotting time of fifty-four minutes.

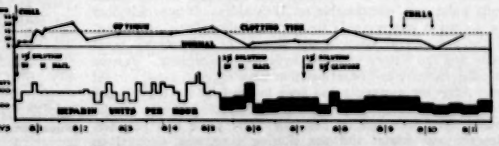



Chart 3 (N. V.; fracture of scapulas and nine ribs on left; embolism seventeenth day).—Heparin chart. The patient had edema on the fifth day from excessive saline intake. The black area indicates the reduction of fluid obtained by doubling the concentration of heparin.

Chart 5 shows the effect on the clotting time of 104 injections over a period of twelve days. Injections were made every two hours for three days, and every three hours thereafter. Clotting times were determined just before an injection and ten

10. Luccia, S. P., and Aggeler, P. M.: Heparin and the Blood Coagulation Mechanism, Proc. Soc. Exper. Biol. & Med. 40:1 41-45 (Jan.) 1939.

minutes after, to ascertain the minimum and approximate maximum range. This schedule was possible only because the patient was exceedingly cooperative and did not object to the numerous injections. It will be noted that the clotting time was kept fairly well above fifteen minutes for twelve days by the use of slightly over forty-one 10 cc. vials by the intermittent method, while thirty-eight vials were used in eight

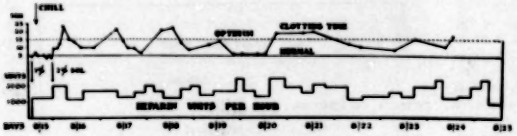



Chart 4 (S. K.; perforated appendix; embolism twelfth day).—Heparin chart.

days when the material was given by continuous drip. On March 22 he was given a light general massage, which was repeated on subsequent days. He was allowed up on March 27, but the heparin was not stopped until March 27, when he was staying up most of the day and walking in the hall. There was no further evidence of embolism and at no time was there abnormal bleeding from the prostatic bed.

We have treated only one case of phlebitis with heparin:

A man of 42 had signs of peritonitis, but he improved on conservative treatment. After one month in the hospital phlebitis of the right leg developed, with severe pain. He was heparinized for six days. During this period there was no progression of the phlebitis and he was more comfortable, although there was no effect on the fever. Several days after the heparin was discontinued, phlebitis appeared in the left leg.

Another case (J. M. in the table) will be reported in detail, because it is the first of its type to be reported. It represents a favorable result from a combination of treatment with passive vascular exercise and heparin in a case of occlusion of the posterior tibial artery:

A white man aged 35 had a positive Wassermann reaction July 22, 1939, and a paretic gold curve December 16. Feb. 10, 1940, he had five hours of fever therapy in the hypertherm, the treatment being over at 2:30 p. m. At 4 p. m. he complained of cramping in both legs. This was relieved somewhat by the injection of calcium gluconate and he went home. The pain in the left leg persisted and he was readmitted to the hospital during the night. Several hours later he was seen by a surgical consultant, who confirmed the evidence of arterial occlusion. The first, second and third toes of the left foot were cold and mottled. Coldness and insensitivity to pinprick extended for 2 inches up on the foot on both dorsal and plantar aspects. There was no pulsation in the posterior tibial artery as compared with a good pulsation on the right. The dorsalis pedis pulse was questionable on both sides. It was felt that the occlusion was probably the result of thrombosis on account of the presence of syphilis, the absence of a detectable heart lesion and the history of recent hypertherm treatment. Passive vascular exercise and heparinization were suggested and carried out. After the extremity had been in the boot for ten minutes there was noticeable improvement in the color of two of the smaller toes, although no posterior tibial pulse was palpable. Heparin was begun and the clotting time was elevated to fifteen minutes. The next morning, after eighteen hours of the combination treatment, the posterior tibial pulse was present, although it was weaker than that of the other side. All of the foot was pink except for a small area about 2 mm. wide at the lateral border of the great toe. Passive vascular exercise was discontinued after one day and heparin was continued for another day. There was no further evidence of circulatory deficiency in the foot. The physical therapy was probably the most important factor in the good result, with heparinization a valuable adjunct.

### POTENCY AND TOXICITY

The potency of heparin obtained from different laboratories may vary markedly. This fact, together with the fact that there is no official standard of potency, causes confusion when results are compared. The unit referred to in this paper is that of the Toronto workers, namely the activity of 0.01 mg. of the crystalline material. Dr. Best[11] believes that the potency of this product is perfectly constant. There is, however, considerable variation in the amounts required for different patients.

In general, the potency in vivo has not been as great as we had expected after reading the previous reports. As indicated in the table, seven patients required approximately 2,000 units an hour to keep the clotting time above fifteen minutes, one required 1,500 units, and three required 1,000 units. The two females in the series were in the last group. The weight of the patients was not significant. Chills and fever, the only toxic effect observed, occurred in the earlier cases, but no such effect was noted in the last five consecutive cases. The price of heparin has come down appreciably since we began using it. The daily cost may not exceed $10 or $15, which is no more than the cost of special nurses.

### DETAILS OF TREATMENT

It is convenient to give the heparin in 2 per cent[12] solution although, if there is indication to restrict fluids, more concentrated solutions may be used. In one case there was no ill effect from repeated injections of the undiluted solution. When the continuous intravenous drip is used, the vein selected may be in the leg or arm. It is more convenient for the patient for the needle to be in the leg, thus leaving both arms free for eating, reading and personal care. In most instances we have inserted a medium size intravenous needle into the vein

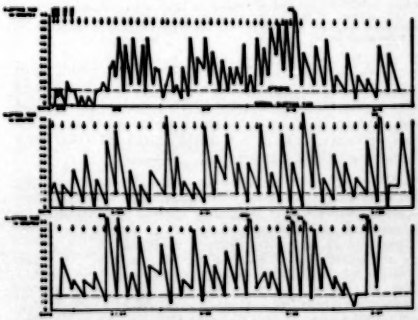


Chart 5 (W. K.).—Effect on the clotting time of repeated intravenous injections of 4 cc. of undiluted heparin solution at intervals of two and three hours over a period of twelve days.

and taped it firmly in place, without the necessity of "cutting down." The leg is not splinted; on the contrary, after a day or two the patient is encouraged to move all extremities at will. In an uncooperative

11. Best, C. H.: Personal communication to the authors.

12. The term "2 per cent" refers to the dilution of the "Solution of Heparin" supplied by the Connaught Laboratories. Since this solution consists of 100 mg. of crystals in 10 cc. of saline (1 per cent) solution, the concentration of crystalline heparin in our "2 per cent solution" is actually only 0.02 per cent.

patient, such as the man with tabetic dementia paralytica in our series, it is essential to fasten a cannula in the vein by ligature. When the patient is sufficiently recovered from his operation or infarction to be ambulatory, the needle may be transferred to a vein in the forearm, after which he may sit in a chair or walk about the room with the intravenous injection running. How long the patient should be ambulatory before the heparin is discontinued is not known; we have felt that two days should be a reasonable period.

SUMMARY

1. Eight patients with postoperative pulmonary embolism have been treated by general heparinization. All recovered, but one required a second course of heparin when a second infarction occurred five days after the first course was ended.

2. Heparin was used with gratifying results in one case of embolectomy of the popliteal artery and one case of probable thrombosis of the posterior tibial artery.

3. The purified heparin that is available at the present time is nontoxic when given intravenously. It is economically feasible to use heparin in the treatment of selected cases.

4. Considerable variation in the amount of heparin necessary to elevate the clotting time to an arbitrary optimum level in different patients has been observed.

## THE INTERPRETATION OF VISIBLE PULSATION IN THE RETINAL ARTERIES

JOHN E. L. KEYES, M.D.
CLEVELAND
AND
WILLIAM F. HATCHER, M.D.
YOUNGSTOWN, OHIO

Our purpose in this communication is to discuss an error that persists in ophthalmic literature concerning the interpretation of pulsation of the retinal arteries.

Two years after Helmholtz [1] announced his discovery of the ophthalmoscope in 1851, Van Trigt [2] and Coccius [3] observed a venous pulsation on the papilla. The following year (1854) Jaeger [4] described an arterial pulse in the retinal arteries and von Graefe [5] noted retinal arterial pulsation in glaucoma. Since then, many observations have been published on pulsation of the retinal blood vessels. The opinion that pulsation of the retinal veins is physiologic, but that pulsation of the retinal arteries is always pathologic, became established in ophthalmic literature and persists to date. When it became possible to observe the fundus of the eye more minutely as the result of improvements in the ophthalmoscope, a few observers expressed doubt that a pulse in the retinal arteries is always pathologic. One of the conclusions of Ballantyne [6] in his comprehensive article, published in 1913, on "Pulsation of the Retinal Arteries" was that pulsation of the retinal arteries is sometimes physiologic. He found an arterial pulse of some kind in 36 per cent of 100 presumably healthy outdoor patients at an eye infirmary and concluded "it is likely that 36 per cent is an under, rather than an over, estimate of the frequency of the pulse."

A survey of eight textbooks on ophthalmology in English, published or revised since 1933, reveals that in five of these books the erroneous statement persists that pulsation of the retinal arteries is always pathologic. No mention was made of the subject of pulsation of the retinal arteries in one book. One author avoided the issue. In only one of the eight textbooks is it clearly stated that pulsation of the retinal arteries is a normal occurrence.

Recent evidence of the persistence of this fallacy is afforded by the 1939 edition of a small textbook of the diseases of the eye which enjoys probably the widest distribution of any ophthalmic textbook in America. Writing of pulsation in the retinal blood vessels, the author of this book states that "pulsation in the veins is often seen in health, but arterial pulsation is always pathological."

The arteries of the retina are not exempt from manifestations of the arterial pulse. The retinal arteries normally function under a mean intra-ocular pressure of 20 mm. of mercury (Schiötz). This intra-ocular pressure does not prevent an arterial pulse but renders it more readily visible. This fact was noted by von Graefe in 1854, when he recorded an accentuation of the arterial pulse, when the intra-ocular tension is increased digitally, or in glaucoma.

Skilful and careful observation will reveal a pulse in at least one branch of the retinal artery in as many as 80 per cent of cases that are suitable for ophthalmoscopic study. Such minute details as movements of the arteries will not be seen in restless, uncooperative patients or in eyes with hazy refractive media or a high degree of simple or compound refractive error.

It is not difficult to observe movement of the retinal arteries with the aid of an electric ophthalmoscope or even with a reflecting ophthalmoscope, employing the direct method of ophthalmoscopy. In many instances a retinal arterial pulse can be seen in the blood vessels near the optic disk through an undilated pupil. The arteries can be examined more minutely and over a larger area of the fundus if the pupil is dilated. As an aid to the beginner in ophthalmoscopy, digital pressure on the anesthetized eye, or through an eyelid, is helpful in that it accentuates the amplitude of the arterial pulse. A pulse wave of good amplitude can usually be seen in the eyes of a person suffering from aortic valvular disease.

To avoid error due to inexperience and difficulties, such as confusing retinal light reflexes, we recommend acceptance of only those ophthalmoscopic details seen by two or more observers, which has been our practice for several years.

Pulsation of a retinal artery has been observed on the disk, in the retina near the papilla and in its visible peripheral branches. The most favorable place to see pulsation is at a bend in the course of a tortuous artery. At such a location a decided lateral movement of the artery synchronous, or nearly so, with the radial pulse is usually visible. Close observation of the movement of a retinal artery in the region of a bend or curve reveals that the movement of the vessel is toward the convexity of the curve. At an S curve this movement is particularly noticeable because it travels in opposite directions. A pulsating forward and lateral movement

From the Institute of Pathology and Department of Surgery, Ophthalmological Service, Western Reserve University School of Medicine, and Youngstown Hospital.

1. Helmholtz, Hermann: Beschreibung eines Augen-Spiegels zur Untersuchung der Netzhaut im lebenden Auge, Berlin, A. Förstner, 1851.
2. Van Trigt, A. C.: The Ophthalmoscope, Nederl. Lancet **2**: 417, 1853.
3. Coccius, Ernestus: Ueber die Anwendung des Augen-Spiegels, Leipzig, I. Müller, 1853.
4. Jaeger, Eduard: Ueber die sichtliche Bluthewegung im menschlichen Auge, Wien. med. Wchnschr. **4**: 36, 51 and 69, 1854.
5. von Graefe, Albrecht: Vorläufige Notiz über das Wesen des Glaukoms, Arch. f. Ophth. (pt. 1) **1**: 371, 1854.
6. Ballantyne, A. J.: Pulsation of the Retinal Arteries, Ophthalmoscope **11**: 271, 338 and 460, 1913.

of an artery synchronous with the pulse is frequently observable at a bifurcation. The most common evidence of an arterial pulse wave is a rapid lateral movement and slower recoil of a vessel. There is, however, also an expansile movement of the arteries which manifests itself by an alternate widening and narrowing of the arterial light reflex. This expansile pulse is usually the only type of pulsation visible in a straight artery. In healthy persons the locomotor type of pulsation is more easily seen than the expansile type. The rarest type of pulsation is the capillary pulse. It is manifested by an alternate flushing and paling of the papilla and may be seen in persons with aortic insufficiency.

In considering the various types of pulsation seen in the retinal arteries, it should be remembered that they are manifestations of an expansile and elongating effect, produced in the relatively unsupported retinal arteries by the passage of the systolic pulse wave. While the cause of the pulsation is constant, the effect varies in straight or tortuous portions of the arteries.

It is not within the scope of this paper to discuss the pathologic conditions in which the normal pulse of the retinal arteries may be altered. Suffice it to state that certain general and local diseases alter the character of the retinal arterial pulse.

SUMMARY

A visible pulse in the retinal arteries is a common physiologic phenomenon. This varies with general and local disturbances of circulation and of the eye. Statements to the effect that pulsation of the retinal arteries is always pathologic should be corrected in textbooks of ophthalmology.

## THE TREATMENT OF DELAYED MENSTRUATION WITH PROSTIGMINE

### A THERAPEUTIC TEST FOR EARLY PREGNANCY

SAMUEL SOSKIN, M.D.
HANS WACHTEL, M.D.
AND
OSCAR HECHTER, B.S.
CHICAGO

In a recent study[1] it was found that the various component phenomena of estrus in the rat may be classified in two categories: (1) the specific proliferative effects of estrogen and (2) those effects which are secondary to hyperemia. The latter effects can be reproduced by nonspecific hyperemic agents such as yohimbine. However, when they result from the action of estrogen they are due to the acetylcholine-liberating properties of this hormone, as demonstrated by Reynolds.[2]

In view of the large proportion of the estrous phenomenon in animals which is dependent on hyperemia, it seemed likely that the role of hyperemia was probably even more important in the periodic menstrual bleeding of the human female. Considering the mechanism of this hyperemia, it would presumably also be under the influence of at least the parasympathetic nervous system. This relationship of the nervous system to uterine hyperemia might readily account for the well known influence of mental, emotional and physical strain on the menstrual history of women. It thus appeared possible that cases of delayed menstruation, now generally ascribed to temporary endocrine dysfunctions, might in fact occur despite normal hormone secretion and be due to abnormally decreased vascular responsiveness. It therefore seemed worth while to attempt to treat such cases by pharmacologic rather than by endocrine means.

TABLE 1.—*The Lack of Effect of Prostigmine on Pregnancy in Rats*

| Number of micrograms of prostigmine per 100 Gm. of body weight injected subcutaneously, on each of the first three days of pregnancy | Approximate Dose Used in Human Beings 2.5 | 5.0 | 10.0 | 15.0 | 20.0 | 30.0 | Approximate Minimum Lethal Dose 40.0 |
|---|---|---|---|---|---|---|---|
| Number of impregnated rats injected at each dosage level | 1 | 1 | 3 | 1 | 4 | 5 | 5 |
| Number of rats which had normal gestation periods and deliveries and bore healthy litters | 1 | 1 | 3 | 1 | 3 | 3 | 0 |
| Number of rats killed by the dosage used | 0 | 0 | 0 | 0 | 1 | 2 | 5 |

### METHODS AND RESULTS

The mechanism of the hyperemic action of estrogen suggested the use of acetylcholine. But, since this seemed not without danger, it was decided to potentiate the naturally occurring acetylcholine in the uterine endometrium by inhibiting the cholinesterase with prostigmine methylsulfate, a synthetic physostigmine-like substance which is commercially available.[3]

Since we proposed to use prostigmine to precipitate the menstrual flow of women in whom this function was significantly delayed, we considered the probability that some women would present themselves in early pregnancy. Although this possibility could be ruled out by history and physical examination in most cases, it was necessary to be certain that the treatment would not disturb an early pregnancy if the diagnosis should be missed. For this purpose a series of freshly impregnated rats was used. The animals were injected on the first three successive days of pregnancy with amounts of prostigmine which varied from doses equivalent to those we wished to use on patients to large doses within the lethal range. The results are summarized in table 1. It may be seen that prostigmine did not terminate the pregnancy in a single instance, even when relatively huge amounts of the drug were given. Those animals which did not succumb to the immediate general effects of the lethal dosage went on to normal gestation periods and deliveries and bore healthy litters.

With the assurance gained from our animal experiments, we proceeded to test the effects of prostigmine on women in early pregnancy, as judged by history, physical examination and a positive Friedman (modification of the Aschheim-Zondek) test. Table 2 shows that the pregnancies were not affected. No untoward or unpleasant, subjective or objective effects of the drug were observed.

Table 3 summarizes the results of prostigmine treatment in cases of delayed menstruation in which early

From the Department of Metabolism and Endocrinology, aided by the Joseph G. Snydacker Fund, Michael Reese Hospital.
Dr. A. S. Tulsky gave the authors permission to cite some of the cases used in this work.

1. Hechter, Oscar; Lev, Maurice, and Soskin, Samuel: The Relation of Hyperemia to the Action of Estrin, Endocrinology 26:73-79 (Jan.) 1940.

2. Reynolds, S. R. M.: Acetylcholine Content of Uteri Before and After Administration of Estrin to Ovariectomized Rabbits, J. Physiol. 95:258-268 (March 14) 1939.

3. Prostigmin methylsulfate, supplied by Hoffmann-La Roche, Inc.

pregnancy was ruled out by the history and physical examination, supplemented by the Friedman test when necessary. Prostigmine invariably precipitated the menstrual flow. The flow started as soon as half an hour after the injection in one instance. The longest interval between the last injection and the beginning of the flow was seventy-eight hours. The average time which elapsed was twenty-eight hours. In some instances the amount of flow was somewhat heavier than that usually experienced by the patient, though not alarmingly so. With one exception, all the patients reported normal menstruation at their next regular period.

### COMMENT

We are aware of the possibility that some of our patients with delayed menstruation might have started to menstruate even if no treatment had been given or if a placebo had been employed. But the invariable nature of our results and the fact that the flow started after an average interval of only twenty-eight hours can leave no doubt that prostigmine precipitates menstruation when it would otherwise not occur. Indeed, from our experience it is possible to assure the patient treated with prostigmine that she will soon menstruate unless she is pregnant. If she fails to menstruate, pregnancy may be diagnosed with the same degree of accuracy as is possible with the Friedman test.

It must be emphasized that this procedure applies only to delayed menstruation in women who have had a normal menstrual history up to the last period. It does not apply either to early or to prolonged amenorrhea due to endocrine dysfunction or to local organic changes. For the sake of completeness we have administered prostigmine in a considerable number of cases of the latter types, without the slightest result.

TABLE 2.—*The Lack of Effect of Prostigmine on Pregnancy in Women*

| Case | Age, Years | Gravidity | Menstrual Delay, Days | Physical Manifestations* | Friedman Test | Prostigmine Dosage† | Result |
|---|---|---|---|---|---|---|---|
| 1. K. B. | 28 | 0 | 11 | S e | + | 3 × 2 cc. | 0 |
| 2. E. S. | 31 | 0 | 11 | S e | + | 3 × 2 cc. | 0 |
| 3. B. J. | 36 | 0 | 12 | S | + | 2 × 2 cc. | 0 |
| 4. L. A. | 21 | 0 | 14 | S E | + | 3 × 2 cc. | 0 |
| 5. M. M. | 38 | II | 14 | ..... | + | 4 × 2 cc. | 0 |
| 6. P. R. | 23 | II | 14 | S E | + | 3 × 2 cc. | 0 |
| 7. K. E. | 36 | II | 14 | S E | + | 2 × 2 cc. | 0 |
| 8. M. B. | 29 | 0 | 14 | S E | + | 3 × 2 cc. | 0 |
| 9. L. E. | 30 | 0 | 14 | S e | + | 3 × 2 cc. | 0 |
| 10. M. S. | 39 | I | 14 | S | + | 3 × 2 cc. | 0 |
| 11. S. M. | 23 | I | 15 | S | + | 3 × 1 cc. | 0 |
| 12. V. H. | 24 | 0 | 16 | S | + | 3 × 2 cc. | 0 |
| 13. A. M. | 34 | 0 | 16 | S | + | 3 × 2 cc. | 0 |
| 14. D. P. | 26 | 0 | 17 | S e | + | 3 × 2 cc. | 0 |
| 15. L. F. | 42 | 0 | 19 | ..... | + | 3 × 2 cc. | 0 |
| 16. J. K. | 24 | 0 | 21 | S | + | 3 × 1 cc. | 0 |
| 17. H. J. | 26 | 0 | 21 | S e | + | 3 × 2 cc. | 0 |
| 18. O. S. | 24 | I | 24 | S E | + | 3 × 2 cc. | 0 |
| 19. E. I. | 22 | II | 26 | ..... | + | 3 × 2 cc. | 0 |
| 20. M. N. | 36 | 0 | 27 | ..... | + | 3 × 2 cc. | 0 |
| 21. K. L. | 26 | I | 29 | S E | + | 3 × 2 cc. | 0 |
| 22. B. W. | 35 | 0 | 32 | S E | + | 2 × 2 cc. | 0 |
| 23. K. S. | 18 | 0 | 42 | S E | + | 3 × 2 cc. | 0 |

* S = softening of cervix; E = enlargement of uterus; s = slight softening of cervix; e = slight enlargement of uterus.

† 3 × 2 cc. indicates that the patient was injected intramuscularly, with 2 cc. of 1:2,000 solution of prostigmine methylsulfate on three successive mornings.

1. The important role of hyperemia in the estrous phenomenon suggested that delayed menstruation might be due to lack of vascular response rather than to endocrine dysfunction.

2. On the basis of the physiologic mechanism of estrous hyperemia, women suffering from delayed menstruation were treated with prostigmine. Menstrual flow invariably resulted.

TABLE 3.—*Initiation of Menstrual Flow by Prostigmine in Cases of Menstrual Delay (Nonpregnant)*

| Case | Age, Years | Gravidity | Menstrual Delay, Days | Physical Manifestations* | Friedman Test | Prostigmine Dosage† | Result‡ |
|---|---|---|---|---|---|---|---|
| 1. K. S. | 19 | 0 | 3 | .... | ..... | 1 × 1 cc. | + (4 hrs.) |
| 2. K. S. | 19 | 0 | 5 | .... | ..... | 1 × 2 cc. | + (6 hrs.) |
| 3. K. St. | 28 | 0 | 5 | .... | ..... | 1 × 2 cc. | + (24 hrs.) |
| 4. L. W. | 22 | 0 | 7 | .... | ..... | 1 × 2 cc. | + (11 hrs.) |
| 5. K. St. | 28 | 0 | 8 | .... | ..... | 1 × 2 cc. | + (10 hrs.) |
| 6. M. B. | 29 | 0 | 8 | .... | ..... | 1 × 2 cc. | + (12 hrs.) |
| 7. M. S. | 27 | 0 | 9 | .... | ..... | 3 × 2 cc. | + (24 hrs.) |
| 8. K. L. | 25 | I | 9 | I | ..... | 1 × 2 cc. | + (½ hr.) |
| 9. M. M. | 22 | 0 | 10 | .... | ..... | 3 × 1 cc. | + (10 hrs.) |
| 10. K. M. | 32 | II | 10 | .... | ..... | 1 × 1 cc. | + (24 hrs.) |
| 11. K. H. | 24 | 0 | 10 | .... | ..... | 3 × 2 cc. | + (24 hrs.) |
| 12. K. B. | 32 | 0 | 12 | .... | ..... | 3 × 2 cc. | + (2 hrs.) |
| 13. H. B. | 20 | 0 | 12 | .... | ..... | 3 × 2 cc. | + (48 hrs.) |
| 14. L. H. | 26 | 0 | 14 | .... | ..... | 1 × 2 cc. | + (48 hrs.) |
| 15. A. D. | 28 | IV | 14 | .... | ..... | 1 × 2 cc. | + (36 hrs.) |
| 16. M. H. | 38 | I | 14 | .... | Neg. | 2 × 2 cc. | + (48 hrs.) |
| 17. M. S. | 19 | 0 | 14 | .... | Neg. | 2 × 2 cc. | + (10 hrs.) |
| 18. P. S. | 30 | I | 14 | s e | Neg. | 3 × 2 cc. | + (36 hrs.) |
| 19. T. B. | 28 | I | 15 | e | ..... | 2 × 2 cc. | + (24 hrs.) |
| 20. L. B. | 20 | I | 16 | .... | ..... | 1 × 2 cc. | + (24 hrs.) |
| 21. L. W. | 21 | 0 | 16 | .... | ..... | 1 × 2 cc. | + (16 hrs.) |
| 22. V. H. | 24 | 0 | 16 | .... | Neg. | 3 × 2 cc. | + (30 hrs.) |
| 23. E. Mc. | 24 | 0 | 18 | .... | Neg. | 3 × 2 cc. | + (76 hrs.) |
| 24. K. W. | 24 | 0 | 18 | e | Neg. | 3 × 2 cc. | + (78 hrs.) |
| 25. G. H. | 24 | I | 34 | .... | Neg. | 2 × 2 cc. | + (3 hrs.) |
| 25. L. K. | 24 | 0 | 35 | I | ..... | 3 × 1 cc. | + (72 hrs.) |

* s = slight softening of cervix; e = slight enlargement of uterus; I = infantile uterus.

† 1 × 1 cc. indicates that the patient was injected intramuscularly with 1 cc. of 1:2,000 solution of prostigmine methylsulfate on a single occasion.

‡ The plus sign indicates the initiation of menstrual flow. The figure that follows the sign in each case is the approximate time after the last injection of prostigmine at which the flow started.

3. Preliminary work on animals and on human beings conclusively demonstrated that prostigmine does not initiate menstrual flow when the delay is due to early pregnancy.

4. Prostigmine has no effect on early or prolonged amenorrhea due to endocrine dysfunction or to local organic changes.

5. The constancy of the results in menstrual delay and the lack of effect on pregnancy make it possible to use prostigmine as a combined treatment for menstrual delay and a therapeutic test for pregnancy.

Twenty-Ninth Street and Ellis Avenue.

**March Foot.**—March foot is a linear fracture through the middle of the shaft of a metatarsal bone appearing without the history of a severe injury. It may occur in the second or third metatarsal bones. The condition derived its name from the fact that it was first noted in army recruits following prolonged marching. Clinically it is characterized by swelling of the soft tissue in the dorsal area with pain and tenderness over the involved bone. The condition is usually associated with metatarsus latus and pes valgoplanus and is sometimes seen secondary to the radical operation for hallux valgus. It is believed to be caused by a mechanical insufficiency in the anterior part of the foot which results in an increased loan on the metatarsal bone. In addition, it may be the result of a strain and may occur in civilians as well as in military recruits.—Hauser, Emil D. W.: Diseases of the Foot, Philadelphia, W. B. Saunders Company, 1939.

# THE HYPOTHALAMUS

## PACEMAKER OF METABOLIC AND EMOTIONAL RHYTHM

FOSTER KENNEDY, M.D., F.R.S.E.
Professor of Neurology, Cornell University Medical College
NEW YORK

"One gains the impression that, consistently with its primitive place in the evolution of the brain, the hypothalamus contains the mechanisms of the more primitive psychic and emotional reactions. It plays a part in conditioning moods of elation and depression, and their expression in laughter or weeping. It is concerned with reactions of defence, aggression, suspicion, fear, anger, sex. It ignores refinements of decency and convention, if isolated from the control of its better educated instructor the frontal cortex, which seems to exercise an inhibitory influence on its cruder yet vitally important functions. The exact clinical picture evoked depends no doubt upon the exact pattern of the lesion."

This sketch of some hypothalamic functions was written by a neurologic surgeon, Norman Dott. He continued his statement by saying that we possess little knowledge of the detailed anatomic arrangement of hypothalamic mechanism. However, this idea is so much understated as to be hardly true.

As we have seen during the present meeting, the mamillary areas are concerned with sleep, the anterior part of the hypothalamus with the antidiuretic principles and, despite some differences of opinion among physiologists, the local habitation of the instruments controlling carbohydrate metabolism and even sexual activity has been named. It seems, however, that more emphasis has been placed on position and process than on the rhythmic character of process. And I would advance the notion that not only vegetative functions are controlled in this primitive area but also their innate systole and diastole. The hypothalamus is a neuroglandular instrument in command of vital rhythm. During the two days of this meeting we have become acquainted with the placement of processes situated in an area one three hundredth part the size of the total brain. Writing this before I hear the sapience of my colleagues, I cannot know whether they will speak of the metronomic function which one can see exerted by this antique middle place. The timing of the organism is placed here, influenced somewhat by its intimate connections with newer and also with older and still more primitive sources of power and feeling. To speak, however, of the signs and symptoms produced by various forms of disease affecting this place would be in a sense only to make a kaleidoscope tortured into pattern of the functions and dysfunctions which have been already described by both physiologists and clinicians, and would be over-repetitious as well.

### FUNCTION OF HYPOTHALAMIC AREA

The supreme mystery lies in commonplace phenomena so exquisitely maintained that they excite almost no attention. The regularity of the rhythm of breathing, the constancy of pulse rate, the exact maintenance of body temperature, the beautiful balance of the intake and output of fluid, the cycle of sleep, the integrity of body weight and the imposed periodicity of the menstrual rhythm—all these ebbs and flows are instrumented primarily through the area which we have been considering. And this integrating mechanism of the diffusely working sympathetic, and the discretely working parasympathetic, systems are linked—and perhaps activated—by hormonal messengers, chiefly from the hypophysis, but stimulated and controlled through the subthalamus to the thalamus and thence to the prefrontal cortex. It is not surely possible that the last arrived chieftain can seriously influence the primitive forces innate in a structure as ancient as the hypothalamus. The rhythms of each individual are innate and are built into the organism. They may seem, superficially considered, to be under the influence of the conscious ego. But so do the Atlantic rollers seem to be made by the wind and the weather. These, however, only change the appearance of the top of the roller. The great wave itself, propagating its energy for thousands of miles across the sea, is really made by another force of which the observer cannot be conscious, namely the rotation of the earth.

While much attention has been devoted to the more easily observed metabolic functions of the hypothalamic area, it would seem proper in now closing our session to ask that more attention be given to rhythmic fluctuations in mood and behavior, and of emotional expression, consequent on stimulation or depression of these areas in a manner as yet not understood. One must remember how Foerster produced the symptoms of acute mania when he set in motion a tumor, pressing from below the walls of the third ventricle. And how in another case, when he wiped blood clot from the surface of the third ventricle walls, manic excitement immediately was produced. In fact, Ranson goes so far as to say that "the fact is no longer doubtful that a manic condition can be produced by mechanical stimulation of the oral part of the hypothalamus in man." And Ranson goes on to say that "the manic symptoms cannot be produced from any other spot, such as the walls of the lateral ventricle or the head of the caudate nucleus." On the other hand, interference with the collicular region and the posterior part of the hypothalamus is followed by unconsciousness and sleep.

We have elected at this session to confine our attention to one small area out of the entire neural mechanism. Such specialization makes for accuracy in one direction. It is, however, a thoroughly artificial approach and inadmissible as an approach to the understanding of the total integration of these structures and functions.

### DISEASE OF THE HYPOTHALAMUS

Many observers, as Penfield, believe that "in the thalamus and on the hypothalamus lies the highest representation of the vegetative nervous system." We know that, by the subthalamus, the hypothalamus is linked structurally and functionally with the corpora striata; with the hypophysis by fibers originating from hypothalamic elements, and that the anterior nuclei of the thalamus are linked to the gyri cinguli above and, below, to the mamillary nuclei by the bundle of Vicq d'Azyr; so we must appreciate that hypothalamic disease will paint pictures many of which are not susceptible of being artificially thrust on the hypothalamus itself for explanation. Further, in an area where sympathetic and parasympathetic functions are both represented in their enormous variety we discover stimulating clinical patterns of dysfunction not ordinarily associated together in our minds. For instance,

Read before the Association for Research in Nervous and Mental Disease, Dec. 21, 1939.

we readily accept amenorrhea as part of the picture of abnormal obesity in young women. We somehow see immediately that the same lesion has produced both of these two symptoms, but we do not so readily see that the fluctuations in body weight, the sleeplessness and the amenorrhea of a young woman with cyclothemia are caused by the same lesion that has produced her recurrent manic behavior and mood. Indeed we constantly are asking ourselves "Did the suppression of her menses cause her mental breakdown?" instead of perceiving that the large probability is that the break in the rhythm of her menses has been produced by the same abnormality in structures and in function that has caused the break in rhythm of her emotional life. Mutual antagonisms in functional activity emerge from lesions in this place. For instance it has been shown that solution of posterior pituitary opposes the action of insulin, and it would seem that pitressin cannot control diabetes insipidus in the presence of sleep. And high blood sugar associated sometimes with acromegaly can hardly be influenced at all by insulin and diet. And why do depressed cyclothemic patients experience depressional depths almost inversely as the square of the distance from sleep? We try to make them sleep but, when they do, for some hours afterward they're always the worse for it. Ordinarily they have a diurnal rhythm, much worse on waking in the morning; many of them state that they feel fog lifting from their spirits and minds in the late afternoon and often they are entirely normal throughout the evening. But such people, should they sleep in the afternoon, do not experience their usual betterment in the evening. A like paradoxical antagonism is seen in the production of narcolepsy and cataplexy by a positive emotion like laughter and surprise producing the negation of sudden morbid sleep or muscular tonelessness and falling. Again may one stress how much the hypothalamus is concerned not only with emotional expression (which may be mainly thalamic) but with mood? And it is no accident that postencephalitic children are hypomanic.

114
40

## CAUSATION

Not all hypothalamic syndromes are due to acquired disease, such as injury, infection or the formation of tumor. One of my patients suffering from severe diabetes insipidus had an interesting family history. Her mother and aunt and her mother's mother have all been extraordinarily obese. The grandmother weighed 230 pounds (104 Kg.) and also her father, of 6 feet 4 inches (193 cm.), 368 pounds (167 Kg.). The other children in the family, aged 9 and 11 years, weighed respectively 128 (58 Kg.) and 118 pounds (53.5 Kg.). My patient, aged 17, three years ago weighed 165 pounds (75 Kg.); there developed severe polyuria and polydipsia and her weight dropped to 98 pounds (44.5 Kg.). Her basal rate was minus 18. There has been no evidence of neoplasm and I believe that she suffers from a familial hypothalamic-pituitary defect. Another girl, aged 20, however, after the removal of a severely infected wisdom tooth became subject to sudden attacks of uncontrollable drowsiness, which she noticed came upon her on anger and laughing, especially during the morning hours. These attacks of sudden sleep were often replaced by attacks of her knees giving way when excited, angered, surprised or suddenly amused. The same weakness has occurred in the arms. She has a sudden sensation of intense weakness at these times but is usually able to protect herself by holding on to a table or, as she said lately, clutching the railing that she had been leaning against when excited by a hockey game. Sometimes on laughing she experiences a sensation of darkness coming from the back to the front of the head followed by sudden falling, in which she has occasionally hurt herself. She has also periods of enforced immobilization, during which she can't lift a hand by will or move a foot or speak. These may last half an hour or an hour and sometimes in them she falls asleep for ten minutes. Emotion triggering morbid sleep put one of my patients in an impossible position when he suddenly slept with snores on kissing a girl in a taxi cab, and a patient with acromegaly always yawned in the middle of his own speeches, an involuntary reflex and no sign of grace.

## ILLUSTRATIVE CASES

It would be commonplace to speak before such a body as this of clinical phenomena which have been so often viewed by us all. For instance, one of my patients at Bellevue with tumor involving the floor of the third ventricle producing polydipsia, polyuria, obesity and impotence of long duration had a psychosis indistinguishable from dementia paralytica; a child with supra-optic glioma characterized by progressive blindness and intense diabetes insipidus, which could be modified by the use of pitressin. Such symptoms have been well recognized and have been much explored already at this meeting. I have seen, however, four families, unrelated to one another, all presenting in the majority of their members clear signs of abnormal pituitary function. In these four families, instances of Froelich syndrome, gigantism, acromegaly, mild diabetes insipidus, occurred; in all four families as well there were two or more cases of manic-depressive psychosis, so that I came to relate in my mind these conditions together. However, not only is manic-depressive psychosis found in frequent association with hypophysial and hypothalamic abnormality but various behavior problems, lying, stealing, arson and temper tantrums, have occurred in young people under my observation, accompanied by functional hypothalamic "organic" signs more frequently than they do in persons physically normal. Such instances are important in the consideration of body-mind relationship.

In this regard the disturbance of vegetative function in hypothalamic encephalitis can hardly be overstated; not only have such cases been difficult to differentiate from so-called pure psychoses but some of them have furnished, by the disruption of vital rhythm, valuable data for a comprehension of neurotic and psychotic phenomena on a physical rather than on a purely emotional or psychic basis.

H. G., a man aged 21, served as a private in the United States Marines during the last war and was supposed to have disintegrated mentally following an alleged attack of influenza in London during the month after the armistice. He was placed in an excellent hospital for mental diseases for about eight months after his return home. The diagnosis was dementia praecox, at that time still the fashionable name for schizophrenia. The clinical picture seen in the spring of 1921 was sufficiently confusing; a young man of splendid physique carried his height of 6 feet 2 inches (188 cm.) with a pronounced stoop, an acquisition of his illness. Without syphilis the pupils were distinctly sluggish to light; the right side of the face flattened in its creases, and there was a fine aspic jelly-like, but definite, nystagmus on lateral conjugate deviation of the eyes to the right or left. There was pronounced tremor in the extended hands. He had lost more than 30 pounds (13.6 Kg.) since his illness; except for the absence of the abnormal reflexes, great increase in the arm, knee and ankle reflexes and involun-

tary shivering movements of the pectoral muscles, nothing more of pathologic interest could be made out in the sensorimotor system. He suffered, however, from severe nocturnal insomnia, rarely sleeping more than two hours before dawn, after which he would usually waken and again grow drowsy and perhaps sleep three or four hours before noon. Whether he slept or not, during the first part of the day he was utterly inert and exasperated by his inertia. He had the utmost difficulty in accomplishing through defective will power and indecision simple acts, such as shaving, dressing or bathing. He agonized for hours in futile efforts to write a short note or keep an important engagement during this early part of the day. In his mental attitude there was no trace of negativism; he desired passionately to do those things which he could not do at that time but which later in the day he often could do with relative ease. There was a distinct resemblance between his inability to perform acts to the completion of which he was urged by will, lacking the stronger adjuvant of emotion, and the palsy of purely voluntary movements in midbrain encephalitis of the parkinsonian type—palsies so often abolished by emotional stimulation. He complained frequently of "numb attacks" during which he felt very cold and in which he shivered and his teeth would chatter like a man with a rigor. During these attacks, even in July weather, his rectal temperature was always subnormal, on several occasions being 97 F.; and on his skin were large patches of goose flesh which covered a third of the body area at a time and which, under observation, changed their position like a breeze over still water.

In the same general period but not necessarily and indeed rarely at the same hours, he had attacks of disturbed breathing rhythm of from a quarter to half an hour's duration. During these attacks he felt as thought he could not fill his lungs with air and breathed with all his accessory respiratory muscles from fifty-six to sixty-four times a minute. At other times he experienced what seemed like a spasm of the laryngeal muscles and breathed more and more stertorously and ineffectively so that the lips were cyanosed and the eyes protruded. Phenomena such as these have appeared at times in hysteria, and various physicians had considered them hysterical in this case. This explanation, however, could not account for the patient's abnormal thirst for ice water. He consumed for a period of eighteen months between fifty and sixty tumblers of water every twenty-four hours and had proportionate polyuria.

An analysis of the initial illness in December 1918, which he had always considered influenza, revealed the only symptom to have been severe headache and intense sleepiness by day and by night. Two negative features of value, however, were that he had had no feeling of fever and that he had never reported sick to a medical officer. It is highly unlikely that this could be true of any youthful patient with the influenza which was prevalent in London at the end of 1918. Furthermore, after three or four weeks sleepiness disappeared during the night time and was present only by day, a reversal of the sleep mechanism sufficiently familiar to all students of epidemic encephalitis.

The patient's symptoms during the last eight months of his illness gradually improved to almost normal, with little or no morning inertia, no difficulty with respiration and no rigors; polydipsia was reduced to an intake of only three quarts of water a day.

A boy of 14 had a similar polydipsia and polyuria, tremors in the upper extremities, excessive salivation and similar distressing paroxysmal attacks in which breathing was exceedingly rapid, labored and difficult. At these times there was great emotional distress and suffering. This boy had acute encephalitis in January 1920 with visual disturbance, diplopia, fever and excessive insomnia; this was followed for many months by apparent recovery and was gradually succeeded by a rhythmic incessant cough and stammering and thereafter by the distressing symptoms already described.

Another patient, a woman of 28, developed severe hypertrichosis of the face and arms following encephalitis. Great increase in body weight has been a fairly common sequel of that disease as it is of neoplasms interfering with the third ventricle floor. It happens that this disturbance of metabolism was seen in our series mainly in female patients. One patient within half a year gained over 150 pounds (68 Kg.).

**Rhythmic movements, breathing irregularities and eccentric stations may be attributed to disturbance of the toning mechanism of muscles.**

Five patients, all with an early parkinsonian syndrome, had stammering as a sequel to their illness. In one of these cases the disorder accompanied a severe relapse precipitated by a fright occurring two months after the onset of encephalitis. In the other instances stammering appeared from three months to two and a half years after the first symptoms and without any psychic shock. Three patients had rhythmic movements. An encephalitic patient had from the onset of her illness bilateral rhythmic action of the masseters, which gave a champing "subway" movement to the jaws. This was constant during the waking hours and, with her immobile facies and unwinking stare, resembled remarkably the breathing movements of a fish: perhaps a return to an earlier facial aspect!

These movements occurred about once in two or three seconds, were not under control of the will nor varied by attention or emotion and could not be inhibited by any voluntary use of the involved muscles. Their maintained rhythm distinguishes them to some extent from habit spasms, some of which, however, have a striatal origin. I think many cases of hysteria may be in mechanism a retreat by the personality from a cortical to a more primitive reflex level of motor expression and sympathetic discharge, so that hysterical episodes necessarily have the striatal and hypothalamic pattern and color imposed on them by the physiologic mechanism through which they find expression.

One patient had very irregular breathing—both in depth and in rate—accompanied by curious noises which occurred only during sleep. On the other hand, a narcoleptic with lingual dystonia and almost unintelligible speech in his sleep talks fluently and normally well. S. J., fifteen months after apparent total recovery from encephalitis, had a parkinsonian relapse, accompanied by attacks of rapid deep breathing, profuse sweating, lacrimation, salivation and venous congestion of the face. These increased in frequency and at last continued throughout the waking hours, causing intense fatigue. Emotion would initiate them, but when started they could not be stopped until their course was run—usually in a minute or two. There was never any feeling of dyspnea but a sensation that he could not possibly fill the lungs and an intense desire to fill them.

One patient had recurrent vomiting which persisted for three weeks. Several times a day, with or without food in the stomach, expulsive movements occurred; the vomiting was probably in morbid process analogous to the rhythmic movements and breathing spasms just described and also analogous to the hiccup seen in certain cases of encephalitis. Such visceral perversions, however, may be due to parasympathetic explosion. A 12 year old boy had acute anteropulsion of the trunk, so that he looked backward through his legs as Peter Pan looked at the bears. He could walk only by splinting his torso upward by his arm, held rigid on his knee. Another boy, aged 15, maintained when sitting or standing a deviation of the trunk to the left so that the upper part of the trunk was almost at right angles to the pelvis. Neither patient ever fell. At a certain point the active pull would cease, movement would end and the attitude would be maintained. This was a clinical replica of the experiments of Ecker and Brookney and Gerard in which stimulation of the posterior part of the posterior area of the third ventricle wall produced concavity of the spine to the ipsilateral side.

Limitation of parkinsonian symptoms to the upper extremities and to the face was observed twice. This leads one to the probability that individual centers in the corpora striata rerepresent individual spinal segments.

**The rich connection between the basal olfactory regions and the hypothalamus account for the almost constant appearance of intense fear referred sickeningly to the pit of the stomach in uncinate fits and even in the dreamy mental states of temporosphenoidal origin. And there is sound structural basis for the fact that persons passing through morbid internal depressions have perversions or entire abolition of appetite, taste**

and smell. The severe mental and emotional depressions in adolescent girls and young women which we wrongly call anorexia nervosa are explicable in these terms also.

A well known physician under my care after a short acute attack of epidemic encephalitis, characterized typically by stupor, diplopia and slight continued fever, experienced an inability to sleep more than four hours in the twenty-four; he had intense motor restlessness, constant elation, a passion for midnight cabaret parties and bursts of talking and walking lasting for hours at a time, which he stated he could in no way control. This manic phase lasted eight months and was followed by a year of depression, slowed activity of mind and body, and occasional irritability. The manic-depressive psychosis ran its course after about two years from the beginning of his illness and then allowed the patient to resume his normal rather sedate and conscientious personality.

COMMENT

I have described at some length my first case of disturbed vegetative function in the course of epidemic encephalitis, but since that time many instances of dementia praecox-like pictures came to our Neurological Department at Bellevue Hospital and to the Neurological Institute. There have been patients with catalepsy, spontaneous or provoked, with fixed bodily attitudes of bizarre character, with altered personalities fluctuating between docility and paranoid opposition; patients with stereotyped and reiterated words and phrases with persistent closure of the eyelids and retention of urine and feces; garrulity alternating with mutism; ethical defects with flight of ideas and euphoria, and at times markedly antisocial trends. The milder cases, however, presented fantastic neurasthenic symptoms, an agitated anxiety, a loss of confidence and exaggerated shyness and self consciousness with feelings of embarrassment, unreality and much slow mindedness.

Some patients suffered from lack of spontaneity and disappearance of all voluntary activity. The emotional tone was apathetic so that, growing disinterested in business, family or friends, the patient ceased to bother about his condition from sheer apathy and mental powerlessness. Mental asthenia may coincide with hallucinations or delusions of a paranoid character, but more usually there is an irritable nervousness toward himself and an inert indifference toward his environment, which for him has become a gray monochrome without significance or form. Such persons usually are sexually impotent, but one sees many instances of greatly increased libido accompanied at times by sadistic behavior. However, in neurology there is happily discerned an inevitability in clinical symptoms emanating from lesions of structures with known physiologic functions. The sympathetic functions after all are centrifugal and centripetal; by their joint action is determined the mood of the organism and they also control smooth muscle contraction and glandular secretion. Lesions therein give rise to dissociation between emotional and voluntary activity of muscle and to alternation in vasomotor control and respiratory rhythm; to emotional mimicry, tachycardia and spastic laughing and crying. Lesions of the hypothalamus and floor of the third ventricle give rise to glycosuria, salivation and increased sweating with maybe pathologic sleep. Tonus in general is under the high control of part of the striatum, and changes in the striatum can give rise to plasticity to the point of catalepsy with tremors and rigidity. Automatic associated movements also are under striatal government: it may be that in paralysis agitans we have an antique expression of both facial emotion and bodily posture: a phylogenic retrogression —man becomes ape.

We have heard the results of physiologic experiment in these brain areas; in epidemic encephalitis these areas are the seat of perivascular round cell infiltration. This is found around the aqueduct also, together with fat accumulation in the ependymal cells of the lateral ventricles and in the tuft cells of the choroid, and throughout the walls and floor of the third ventricle.

I submit that we must correlate these lesions with disorders of personality as we correlate lesions of the thalamus and striatal bodies with athetosis, tics and tremors. By so doing we shall take a notable step toward developing knowledge of the metabolic rhythm and may even lay the foundation of the science of the pathology of emotional and energic drives.

410 East Fifty-Seventh Street.

## PHOTOSENSITIZATION BY PHENOTHIAZINE

FLOYD DeEDS, PH.D.
ROBERT H. WILSON, PH.D
AND
J. O. THOMAS, A.B.
SAN FRANCISCO

Among the more promising organic insecticides developed as substitutes for lead and arsenic is phenothiazine. When field tests were made on the practical application of this insecticide for control of the codling moth, some of the men applying a spray containing the compound complained later of intense itching, irritation and reddening of the skin. In some cases the reactions were severe, being accompanied by edema and secondary infection in areas of intense hyperemia, and required hospitalization. Attending physicians have diagnosed the reaction variously as sunburn, chemical burn and dermatitis.

In sharp contrast to these reports is the fact that several members of our laboratory staff have worked with phenothiazine for several years on an investigation of its toxicity and have experienced no cutaneous reactions. Applications to the forearms of phenothiazine mixed with hydrous wool fat to promote absorption produced no irritation. In an investigation of the efficacy of phenothiazine as a urinary antiseptic,[1] a series of ninety-two patients were given doses of the compound orally, ranging from 3.12 to 42.9 Gm. for the entire period of treatment, but no undesirable cutaneous reactions were produced.

### SUGGESTED EXPLANATION OF CUTANEOUS REACTIONS

In view of these apparently contradictory facts, an explanation of the toxic reactions observed in orchard workers was sought on the basis of the known fate of phenothiazine in the body [2] and the environmental conditions of the workers.

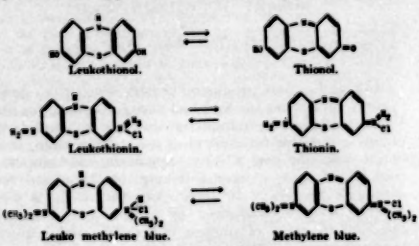
Phenothiazine, after oral administration, is oxidized to the reversible oxidation-reduction system thionol-leukothionol. The products excreted in the urine are unoxidized phenothiazine in some soluble form, thionol,

Contribution 454, Food Research Division.
From the Bureau of Agricultural Chemistry and Engineering, United States Department of Agriculture, at the Department of Pharmacology, Stanford University School of Medicine.

1. DeEds, Floyd; Stockton, A. B., and Thomas, J. O.: J. Pharmacol. & Exper. Therap. 66:353 (April) 1939.
2. DeEds, Floyd; Eddy, C. W., and Thomas, J. O.: J. Pharmacol. & Exper. Therap. 64:250 (Nov.) 1938.

leukothionol, and leukothionol in some chemical combination from which it is readily liberated in acid reaction. In the present connection the reversible oxidation-reduction system thionol-leukothionol is of interest. Thionol is closely related to thionin (Lauth's violet) and to methylene blue, as shown in the oxidation-reduction equations employing structural formulas.

These three oxidation-reduction systems have in common a characteristic which may have some bearing on the problem at hand. In each case, the leuko form kept in solution under strictly anaerobic conditions is photosensitive. On exposure to sunlight, the leuko form is converted to the oxidized component. Likewise the porphyrins and chlorophyll are oxidation-reduction systems in which the leuko form is photosensitive. These systems, including thionol as shown later, sensitize individuals to sunburn. Whether photosensitivity of the leuko forms is essential to the production of sensitization to sunburn cannot be stated, but it is interesting to note that the two phenomena are often associated. In addition to these systems other photodynamic sensitizers are known such as erythrosin, rose bengal, rhodamine, anthracene derivatives, acridine dyes, quinine and hypericin. Still others produce sensitization to sunburn indirectly through their ability to produce porphyrins by an action on the blood.




Examination of a urine sample obtained from an orchard worker who experienced a cutaneous reaction associated with the spraying of phenothiazine showed the presence of thionol and leukothionol. The presence of these two oxidation products of phenothiazine in the urine proves that phenothiazine must have been absorbed into the body from the skin, possibly by swallowing saliva contaminated with phenothiazine, or more likely from the respiratory tract after inhalation of phenothiazine spray.

Orchard workers applying phenothiazine sprays are subjected to environmental conditions contrasting sharply with those of laboratory workers and the ninety-two patients observed by us.[1] The orchard worker is exposed considerably to sunlight and on warm days may strip to the waist, especially in areas such as the Yakima and Wenatchee valleys of Washington. The exposure to sunlight and heat, the demonstrated presence of thionol in the urine indicating absorption of phenothiazine, and the possibility of a photodynamic effect provide a rational explanation of the undesirable cutaneous reactions in the orchard workers exposed to phenothiazine spray. This theory was subjected to the following tests:

### TESTS FOR PHOTOSENSITIVITY

We served as experimental subjects in the following manner: The volar surface of one forearm of each subject was divided by drawing an ink line from the elbow to the wrist, and the area on one side of the line was painted with a 2 per cent alcoholic solution of phenothiazine so as to leave a thin, even deposit of phenothiazine after evaporation of the alcohol. The arm was then exposed to the radiation of a General Electric No. S-1 sun lamp at a distance of 30 inches (76 cm.) in such a manner as to give three areas of different exposure time at right angles to the ink line. This procedure permitted a determination of the exposure time necessary to produce a definite degree of hyperemia in each subject and at the same time show whether the area coated with phenothiazine was more or less susceptible than the corresponding control area. Two subjects (F. D. and R. H. W.) took 0.75 Gm. of phenothiazine in capsules in three divided doses of 0.25 Gm. The third subject (J. O. T.) took capsules of thionol in lieu of phenothiazine. Approximately twelve hours after taking the last dose each subject exposed the volar surface of the other forearm to the radiation of the sunlamp under similar conditions.

The results of these tests may be summarized as follows: The control arm of each subject clearly demonstrated that the area coated with phenothiazine was markedly protected against the development of hyperemia even with the longest exposure. Accordingly it must be concluded that, under the conditions, phenothiazine applied locally caused neither irritation nor predisposition to sunburn. Irradiation of the other arm after oral administration of either phenothiazine or thionol resulted in a sensitization to sunburn as judged by an increased hyperemia in areas receiving the same amount of radiation as the corresponding areas on the control arms. It must be kept in mind that the effects observed necessarily represented a hyperemic area developing about eighteen hours after that on the control arm.

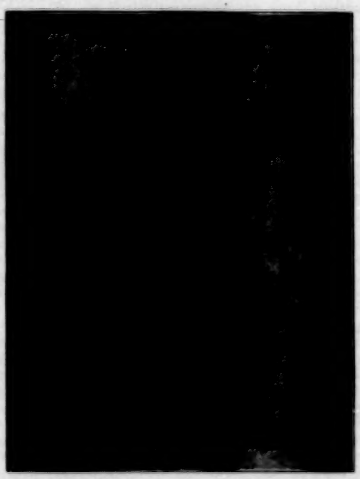
The results obtained on subject R. H. W. are shown in the reproduction of the photograph. To accentuate the results for purposes of reproduction the photograph was made with color blind film so as to insure darkened areas where hyperemia existed. This procedure resulted in the reproduction of freckles as black spots. The ulnar aspect of the volar surface of the left arm shows the lack of hyperemia due to the protective action of locally applied phenothiazine. The radial aspect of the same arm shows three areas of hyperemia due to three different exposure times. The dark band across the volar surface of the right arm shows the more intense hyperemia produced after oral administration of phenothiazine. The exposure time was the same as that for the area of most marked hyperemia on the left arm.

These results strongly suggest that the undesirable reactions experienced by orchard workers when applying phenothiazine sprays are not due to a local irritant action of phenothiazine. More probably they are due to a systemic reaction of the individual to sunlight traceable to a photosensitization produced directly or indirectly by the presence of the oxidation-reduction system thionol-leukothionol in the tissues resulting from the oxidation of absorbed phenothiazine.

If this is true, several remedial measures suggest themselves: 1. Prevent absorption of phenothiazine by wearing a suitable mask. 2. Eliminate undue exposure to sunlight by wearing suitable clothing. 3. Protect exposed areas from sunlight by protective coatings such as zinc oxide ointment or even phenothiazine itself. It should be mentioned that our experiments were made with pure phenothiazine and permit no conclusions regarding the action of possible impurities or other

ingredients in the spray. Lastly, a victim of such photosensitization should, in addition to any soothing local application advised by the attending physician, remain in a dimly lighted room and drink liberal quantities of water to promote diuresis and thereby facilitate excretion of the thionol.

With regard to the mechanism of the photosensitization, two possibilities suggest themselves: The thionol may produce sensitization per se in the same sense that coproporphyrin does or it may give rise to an increased porphyrin content of the blood, as is probably the case with certain other sensitizing agents. Attempts made by us to determine whether or not oral administration of phenothiazine leads to an excretion of coproporphyrin were inconclusive. The method employed for the detection of coproporphyrin in urine depends on observation of the absorption bands in 25 per cent hydrochloric acid. Unfortunately for such identification, thionol



Photosensitization produced by orally administered phenothiazine (subject R. H. W.).

is excreted in the urine, and the absorption bands of thionol in 25 per cent hydrochloric acid are so nearly the same as those of coproporphyrin that we were unable to differentiate the two substances with our spectroscope.

### SUMMARY AND CONCLUSIONS

1. Oral administration of phenothiazine results in the excretion of the reversible oxidation-reduction system thionol-leukothionol.

2. Leukothionol is photosensitive and, under anaerobic conditions, is oxidized to thionol when exposed to sunlight.

3. Oral administration of phenothiazine to two persons and thionol to one person resulted in a demonstrable sensitization to radiation.

4. It is suggested that the cutaneous reactions of orchard workers applying phenothiazine sprays are due to photosensitization and not to local irritation by phenothiazine.

## SUPPRESSION OF ISO-AGGLUTININS

### AND THE SIGNIFICANCE OF THIS PHENOMENON IN SERUM TRANSFUSIONS

SIDNEY O. LEVINSON, M.D.
AND
ANNY CRONHEIM, M.D.
CHICAGO

Universal donors (group O) are used very commonly for patients belonging to other blood groups. There is a theoretic risk of incompatibility from the use of universal donors whose serum iso-agglutinins are of high titer. Gesse [1] collected forty-six instances of incompatibility resulting in twenty deaths following the use of blood from a universal donor. On the basis of agglutinin titrations he found that more than 30 per cent of universal donors have an agglutinin titer over 1:32, a titer which he considers dangerous. It is obvious that practical experience does not confirm these fears. Vast numbers of transfusions from universal donors are given with complete safety. The rare occurrence of an incompatibility reaction is more apt to be due to inaccurate blood grouping from the use of weak typing serums and weak agglutinogen. Erroneous blood grouping is a more frequent cause of incompatibility.[2]

Why can serum containing iso-agglutinins against the recipient's cells be administered safely? Dilution of the agglutinins [3] is not an adequate explanation. Wiener [4] points out that absorption of the donor's agglutinins by the tissues of the recipient [5] and neutralization by the recipient's own serum will also tend to prevent a reaction. However, there are no quantitative studies on this absorption effect. The significance and degree of agglutinin suppression has not received sufficient attention or emphasis.

Recent developments in the use of serum or plasma for transfusions focus attention on the importance of agglutinin absorption. Two reports [6] on the use of plasma transfusions comment briefly that no typing or compatibility tests were performed and no reactions were observed. No explanation, however, is offered for the fact that compatibility tests may be omitted with impunity.

Large amounts (from 100 to 1,000 cc.) of pooled human serum have been administered intravenously by us in the past ten years in more than 1,000 instances, without any evidence of incompatibility. We have always employed pooled human serum (each pool made up of the serum from thirty to fifty different specimens

From the Samuel Deutsch Serum Center.

1. Gesse, E. R.: The Nature and Treatment of Hemolytic Shock After Blood Transfusion, Vestnik khir. **43**: 59, 1935; Ueber die Verwendung des sogenannten Universalspenders bei der Bluttransfusion, Deutsche Ztschr. f. Chir. **245**: 371, 1935. Hemolytic Shock After Blood Transfusion, Editorial, J. A. M. A. **106**: 2241 (June 27) 1936.

2. Wiener, A. S.: Blood Groups and Blood Transfusions, ed. 2, Springfield, Ill., Charles C. Thomas, Publisher, 1939.

3. Ottenberg, Reuben: Studies in Iso-Agglutination: I. Transfusion and the Question of Intravascular Agglutination, J. Exper. Med. **13**: 425, 1911.

4. Wiener: Blood Groups and Blood Transfusions, footnote, p. 49.

5. Kritschewski, J. L., and Schwarzmann, L. A.: Die gruppenspezifische Differentierung der menschlichen Organe, Klin. Wchnschr. **6**: 2081 (Oct. 29) 1927; ibid. **7**: 896 (May 6) 1928. Witebsky, E.: Ueber gruppenspezifische Organunterschiede beim Menschen, ibid. **7**: 118 (Jan. 15) 1928; Ueber die Antigenfunktion der alkohollöslichen Bestandteile menschlicher Blutkörperchen verschiedener Gruppen, Ztschr. f. Immunitätsforsch. u. exper. Therap. **49**: 517, 1927. Witebsky, E., and Okabe, K.: Ueber den Nachweis von Gruppenmerkmalen in den Organen des Menschen, ibid. **53**: 359, 1927.

6. Tatum, W. L.; Elliot, J., and Nesset, N.: A Technic for the Preparation of a Substitute for Whole Blood Adaptable for Use During War Conditions, Mil. Surgeon **85**: 481 (Dec.) 1939. Strumia, M. M.; Wagner, J. A., and Monaghan, J. F.: Treatment of Secondary Shock, J. A. M. A. **114**: 1337 (April 6) 1940.

of blood). We have observed that large pools of serum never showed rich agglutinin content, whereas many of the individual serums that made up the pool possessed a high agglutinin titer.

We determined to study the agglutinin absorbing action of serum. The tube-slide method was employed. Blood cells were suspended in 0.85 per cent sodium chloride solution. Equal amounts (0.5 cc.) of serum or diluted serum and suspended cells were mixed in a test tube, and after due agitation a sample was removed with a glass rod, placed on a glass slide and examined under a microscope periodically up to thirty minutes after preparation. All the results reported at this time were obtained at room temperature, with controls in the incubator and refrigerator.

Two rows of serum dilutions were set up. In the first row the test serum was diluted with physiologic solution of sodium chloride, while in the second row the test serum was diluted with serum of the opposite group. Thus when group A serum was employed as the test serum, group B serum was used for diluting purposes against the saline dilution as control. When group B serum was used as the test serum, group A serum was the diluent against a saline control. Nineteen serums were tested, as summarized in the accompanying table. The average agglutination observed with the controls of serum diluted with saline solution was 1 to 20+. The average agglutination in the serum diluted with serum was 1 to 2. Two of the twenty serums which we used were very weak in agglutinins,

*Suppression of Iso-Agglutinins*

| Test Serum | | Type of Diluting Serum | Type of Cells | Agglutination Titer in | |
|---|---|---|---|---|---|
| Number | Type | | | Saline Dilution | Serum Dilution |
| 1 | A | B | B | Over 18 | 3 |
| 2 | A | B | B | 9 | 1 |
| 3 | A | B | B | 40 | 0 |
| 4 | A | B | B | 12 | 3 |
| 5 | A | B | B | 12 | 1 |
| 6 | A | B | B | 6 | 1 |
| 7 | B | A | A | 50 | 3 |
| 8 | B | A | A | 18 | 3 |
| 9 | B | A | A | 9 | 1 |
| 10 | B | A | A | 21 | 6 |
| 11 | B | A | A | Over 80 | 3 |
| 12 | B | A | A | 24 | 3 |
| 13 | B | A | A | 12 | 1 |
| 14 | B | A | A | 3 | 1 |
| 15 | B | A | A | Over 20 | 0 |
| 16 | B | A | A | Over 30 | 3 |
| 17 | B | A | A | 9 | 3 |
| 18 | B | A | A | 9 | 3 |
| 19 | B | A | A | 15 | 3 |
| Average | | | | 21 | 2 |

so that no agglutination occurred in the saline dilution beyond 1 to 3. One serum was very rich in agglutinins, agglutinating cells in a saline dilution over 1 to 80. On the other hand, in two instances in which serum was used as a diluent of the agglutinating serum, no agglutination could be observed in the lowest dilution of 1 to 1. In seven instances in which serum was used as a diluent, no agglutination was observed beyond a 1 to 1 dilution, and in only one instance was there agglutination seen in a dilution of 1 to 6.

### COMMENT

The experiments described demonstrate clearly the agglutinin neutralizing action of serum. This neutralizing property of serum is aided by a like property of all the body cells. This matter is under investigation at present. Neutralization of agglutinins by both tissue and serum of the recipient provides a wide margin of safety in protecting the recipient's red blood cells from the infused agglutinins. This mechanism of agglutinin absorption not only accounts for the practicability of using universal donors but also explains the safety of serum or plasma transfusions without preliminary blood grouping and compatibility tests.

Since there is neutralization of agglutinins in vitro when different groups of serums are mixed, it is recommended that serum or plasma prepared for transfusions should be made up of pools containing all blood groups, resulting in a final low agglutinin titer fluid.

## *Clinical Notes, Suggestions and New Instruments*

### RECURRENT HERPES OF THE CORNEA AND RECURRENT HERPETIC FEVER

#### RESULTS OF TREATMENT WITH SMALLPOX VACCINE

PERK LEE DAVIS, M.D., PHILADELPHIA
Assistant Attending Physician, Philadelphia General Hospital

There are many diseases caused by viruses. They occur in plants, for example the mosaic disease in tobacco and the rosette disease in wheat. They are found in birds as in parrot fever and in animals as in equine encephalomyelitis, rabies and foot and mouth disease, which types may also affect man. In man there are many infectious fevers caused by these virus agents. Among these may be mentioned smallpox, measles, chickenpox, epidemic influenza, infantile paralysis, encephalitis, benign lymphocytic choriomeningitis, herpetic fever, herpes zoster and the common cold.

Although recovery from many virus diseases gives an immunity which lasts for years, it is not constant. It is well known that the common cold, herpes labialis and influenza do not protect the individual from subsequent attacks.

All viruses are intracellular parasites, and a number of them give rise to "coccoid bodies" within the cells which they infect. It has been shown that the number of these bodies is a fair index of the infectivity of a virus. These inclusion bodies, or Lipschutz granules, are within the nuclei of the epithelial cells of all herpetic blisters. They bear a striking resemblance to the Guarnieri bodies in smallpox, which are situated in the protoplasm of the cells. Since vaccinia virus protects individuals from smallpox, it was thought that it might be useful in resistant herpetic conditions.

This paper is concerned with the results of treatment with smallpox vaccine of three patients with herpes of the cornea and eleven patients with recurrent herpetic fever. These fourteen patients were seen in private practice, in the wards of the Philadelphia General Hospital and in the Barton Dispensary of the Woman's Medical College Hospital. Since the results have been uniformly successful in all fourteen cases, only one case of each type will be described in detail. Suffice it to say that, except for minor details as to the duration and frequency of the condition and the number of vaccinations necessary, they were all essentially similar. The treatment seemed to be simple, effective and dramatic in its results.

### REPORT OF CASES

CASE 1.—A man aged 44 in 1925 complained of a herpetic ulcer in the left cornea which had persisted for six weeks. This attack was preceded by a severe herpes labialis which had been present for two months before the corneal lesion developed. From 1925 to 1930 he had had three similar recurrences of herpes labialis followed by herpes of the cornea and subsequent ulceration. The last ulcer in 1930 persisted for four months, with continuous herpes of the lips. At this time he was under the care of a prominent ophthalmologist, who had had various presumptive foci removed. The patient then remained well for

more than five years, but in October 1936 a herpetic lesion developed on the face. Since this manifestation always preceded involvement of the eye by about two months, he consulted a dermatologist. However, in fifteen weeks an ulcer developed on the left cornea. Tuberculin tests done at this time gave negative results. He was then seen by the ophthalmologist, who reported a superficial keratatis covering the pupillary area with branched vessels at the limbal margin. He responded slowly to local eye treatment. He was well from April until September 1937, when another herpetic lesion developed involving the lips and face, followed by a herpetic ulcer of the left cornea. Several allergists studied him and reported that his reactions to tests would ordinarily be regarded as negative but felt that food sensitivity was a factor, so banana, grapefruit, chocolate, apple and tomato were interdicted. Sinus studies showed cloudiness of the antrums and the ethmoids. Operations on the sinuses and a tonsillectomy were done. In spite of the diet and the operations there was a recurrence in November 1938. His family physician referred him for study. The patient stated at this time that the present lesion on his lips and face had been there for two months and had been refractory to local treatment. He stated that because of the usual sequence an ulcer of the cornea would be expected to occur almost any time. He was profoundly concerned because he was always incapacitated for from two to four months, and from an economic standpoint he had sufficient cause for worry.

Except for the obvious lesions on the lower lip and chin the physical examination was objectively negative. The prostatic smear yielded negative results. Laboratory examinations of the blood, spinal fluid, urine and feces gave negative results. The serologic reaction for syphilis was negative.

He was vaccinated with freshly procured vaccinia virus. The vaccination was repeated at ten day intervals until he had been vaccinated four times. The first, the third and the fourth vaccinations were takes. Fifteen days after the initial vaccination the lesions on the lip and the chin were almost completely resolved. This was the first time since 1925 that a corneal ulcer had not followed the original herpetic lesion. He has been on a regular diet without any food restriction, has been seen every month for a year and has been symptom free. He has gained weight and feels stronger.

CASE 2.—A man aged 30, seen in the service of Dr. Hobart A. Reimann, Philadelphia General Hospital, complained of chronic fatigue and loss of weight for five years. There had been a mild diurnal fever to 100 F. for this period. He complained of pains in his legs and stated that his entire body ached. The most marked feature had been the constantly recurring fever blisters involving the face, lips and nose, which had been most severe since early December 1938. Since this time his weakness, body pains, weight loss and lethargy had been more profound. He had lost 20 pounds (9 Kg.) up to the time that he was admitted in March 1939. On further questioning the patient stated that for the past five years and particularly since November 1937 he had had recurring attacks of herpes of the nose, lips and face, with pains in his back and severe bone pains every month or six weeks. His most recent attacks had been five weeks and two weeks previous to admission.

The physical examination was essentially negative. The blood pressure and pulse rate were normal and showed no orthostatic abnormality. Roentgenographic investigations of the chest, gastrointestinal tract, colon and genito-urinary tract were negative. Laboratory examinations of the gastric contents, feces and urine were negative. An estimation of the blood chlorides, sugar and urea was within normal limits. The serologic tests for syphilis were negative. Repeated examinations of the blood for malarial parasites were negative. The erythrocytes numbered 3,100,000 and the leukocytes 2,550 per cubic millimeter of blood. The differential smear showed 44 per cent polymorphonuclear neutrophilic leukocytes and 66 per cent lymphocytes. The hemoglobin was reported to be 58 per cent of normal. The basal metabolic rate was minus 12. The electrocardiographic tracings were normal. The temperature record showed a mild diurnal rise of fever from 98 to 100 F., with a proportional increase in the pulse rate.

He received six vaccinations with ordinary smallpox vaccine at fourteen day intervals, and all of them were takes. The patient gained 10 pounds (4.5 Kg.) in three weeks. He felt much stronger and the feeling of ennui disappeared. The fever subsided completely in six weeks. When last seen in November 1939 he was 32 pounds (14.5 Kg.) heavier than he had been. He stated that he never felt better.

### COMMENT

An immunity relationship between herpes simplex and smallpox and chickenpox was suggested early in 1927.[1] Schmidt[2] used the herpetic vesicle fluid to vaccinate eight patients with recurrent herpetic infection, with good results. This method is probably more specific, but if extreme care is not taken the danger of infection is increased. Foster and Abshier[3] treated thirty-five patients who had herpes simplex with smallpox vaccine, with only five recurrences. They found that the course of the eruption was decreased in every instance and that immunization to further attacks occurred. Brain[4] believes that the effectiveness of smallpox vaccine in these cases is purely a nonspecific response. Reimann[5] believes that the effect is probably a combination of specific and nonspecific factors.

The author heartily recommends the use of smallpox vaccine in the treatment of recurring herpetic infections. It seems to work best if used every ten to fourteen days for from four to eight times. This method has been employed with success and has proved to be safe, efficient and effectual.

### SUMMARY

1. Smallpox vaccine was used in the treatment of fourteen patients, three with recurrent herpes of the cornea and eleven with recurrent herpetic fever, all with uniformly good results.

2. Ordinary smallpox vaccine is a reliable, safe, efficient and effectual means of treating herpetic conditions.

255 South Seventeenth Street.

## ARTERIOSCLEROSIS OF THE RENAL ARTERY ORIFICES WITH SEVERE HYPERTENSION

CHARLES F. STEWART, M.D., NEW YORK

In a recent discussion of experimental hypertension Goldblatt[1] stated that "during the past year, in a few cases of hypertension without renal arteriosclerosis, severe sclerosis and narrowing of the orifice or lumen of the main renal arteries or the lumen of the larger extrarenal branches, obviously sufficient to cause renal ischemia, have been observed." Leiter[2] reported a case of hypertension believed to be due to sclerosis of the main renal arteries (case 2). The patient's blood pressure varied from 240 to 180 systolic and from 160 to 88 diastolic; the kidneys were very small, one weighing 41, the other only 22 Gm. The glomeruli of the left kidney were hyalinized and numerous tubules were atrophied and obstructed. The main renal arterial branches had an extremely thickened, cellular and fibro-elastic intima; the internal elastica was degenerated. The medium and smaller arteries were the site of extensive degeneration of the elastica and in some of the arteries a new media had developed with a new internal elastic membrane. There was subendothelial

1. Gildmeister, E., and Herzberg, K.: Weitere Versuche über Immunitätsbeziehungen zwischen Herpes und Pocken, Deutsche med. Wchnschr. **53**: 138 (Jan. 21) 1927.

2. Schmidt, F. R.: Vaccination for Herpes, Arch. Dermat. & Syph. **32**: 106 (July) 1935.

3. Foster, P. D., and Abshier, A. B.: Smallpox Vaccine in the Treatment of Recurrent Herpes Simplex, Arch. Dermat. & Syph. **36**: 294 (Aug.) 1937.

4. Brain, R. T.: Biological Therapy in Virus Diseases, Brit. J. Dermat. **48**: 21-36 (Jan.) 1936.

5. Reimann, H. A., in conversation with the author.

From the Department of Pathology, Columbia University College of Physicians and Surgeons.

Drs. Walter W. Palmer and Allen O. Whipple gave the author permission to transcribe the clinical records.

1. Goldblatt, Harry: Experimental Hypertension Induced by Renal Ischemia: Harvey Lecture, May 19, 1938, Bull. New York Acad. Med. **14**: 523, 1938.

2. Leiter, Leo: Unusual Hypertensive Renal Disease? 1. Occlusion of Renal Arteries (Goldblatt Hypertension); 2. Anomalies of Urinary Tract, J. A. M. A. **111**: 507 (Aug. 6) 1938.

hyperplasia of the arterioles with but little hyalinization. Many tubules of the right kidney were greatly hypertrophied; others were obstructed. The glomeruli were enlarged; in some the basement membrane was diffusely thickened; in others there were focal hyalinization, numerous adhesions, lipoid degeneration and rarely acute hemorrhagic inflammation. The alterations of the arteries were essentially the same as described for the left kidney. The veins of the kidneys were normal.

A case was reported by Freeman and Hartley [3] of a man aged 57 with hypertension, presumably on the basis of arteriosclerosis of one main renal artery. Two years before death the patient had his right kidney removed following rupture caused by a fall. Histologically it was normal. In the succeeding sixteen months he was well and several blood pressure readings were normal. Eight months before death, however, his blood pressure was found to be 230/140. At postmortem examination the left kidney weighed 200 Gm. Narrowing the orifice of the left renal artery was a large arteriosclerotic plaque; no narrowing of the renal arterioles was seen. The great majority of the glomeruli were normal; some in scarred areas of the parenchyma appeared to have been recently hyalinized. In the interstitial

Fig. 1.—Hyalinization of glomeruli, pericapsular fibrosis, atrophy of tubules, interstitial fibrosis and leukocytic infiltration (hematoxylin-eosin stain; × 110).

tissue was a moderate polymorphonuclear and mononuclear leukocytic reaction. A few of the tubules contained polymorphonuclear leukocytes.

Leadbetter and Burklund [4] recorded the case of a Negro boy with an ectopic right kidney accompanied by hypertension. With its removal the blood pressure returned to normal. Apparently the cause of the hypertension was a mass of smooth muscle in the lumen of the right renal artery, markedly narrowing its lumen. No evidence of inflammatory or proliferative changes was found in the excised kidney, which was, however, of only half the normal weight.

In reviewing cases of hypertension, Oppenheimer, Klemperer and Moschkowitz [5] found eighteen cases of unilateral narrowing of the renal artery, fifteen of which presented hypertension. There were arteriosclerosis and arteriolar sclerosis of the kidney in every case. These workers think that the intrarenal arterial changes preceded and perhaps accounted for the arteriosclerosis of the main renal arteries.

3. Freeman, Gustave, and Hartley, George, Jr.: Hypertension in a Patient with a Solitary Ischemic Kidney, J. A. M. A. 111: 1159 (Sept. 24) 1938.

4. Leadbetter, W. F., and Burklund, C. E.: Hypertension in Unilateral Renal Disease, J. Urol. 39: 611, 1938.

5. Oppenheimer, B. S.; Klemperer, Paul, and Moschkowitz, Leo: Personal communication to the author.

### REPORT OF CASE

The case reported here is one in which the essential lesion appeared to be sclerosis of the renal arteries.

*History.*—A Jewish deliveryman aged 37, married, had three years before admission passed an examination for life insurance; at that time his blood pressure and urine were normal. Two years later he complained of weakness and a dull headache; he had lost 10 pounds (4.5 Kg.). A month later his systolic blood pressure was 230. He was given, without relief, weekly intravenous injections of an unknown drug by his physician. Moderately severe dyspnea began within a month, and he had edema of the ankles in the afternoon and nocturia (from one to three times). He was told that his heart was "bad" and that he had anemia. During the month before he entered the hospital the weakness increased; he was drowsy and suffered from anorexia, nausea and infrequent vomiting. There was dyspnea after climbing six steps; he also had slight orthopnea and occasional twitchings of the muscles of the arms. He had had gonorrhea in his youth and lobar pneumonia eleven years before admission. An undescended left testicle was removed when he was 16 years old. His mother has hypertension.

*Examination.*—He was well developed, well nourished and slightly dyspneic. The breath was uremic. There were occasional twitchings of the muscles of the hands, feet and lips. The nasal margins of the optic fundi were blurred; the arteries were narrowed and arteriovenous notching was minimal. There was no hemorrhage or exudate. The heart was enlarged, the left border being 1 cm. beyond the left midclavicular line. The second aortic sound was moderately accentuated and louder than the second pulmonic. The liver edge was felt at the costal margin.

*Laboratory Data.*—Hemoglobin was 35 per cent; red blood cells numbered 1,700,000; white blood cells 9,600; polymorphonuclears 79 per cent; lymphocytes 14 per cent; monocytes 6 per cent; eosinophils 1 per cent. The erythrocyte sedimentation rate was 162 mm.; serum protein 7.5 per cent; albumin 4.0 per cent; globulin 3.4 per cent; nonprotein nitrogen 262 mg. per hundred cubic centimeters, and carbon dioxide capacity 25 volumes per cent. The urine was pale and clear with specific gravity 1.010, reaction acid, albumin +++, dextrose 0, casts 0, red blood cells 0, white blood cells occasional clumps. The Wassermann and Kline reactions were ++++. An electrocardiogram showed some slurring of the ventricular complexes in all leads suggesting some fibrosis of the heart muscle.

The blood pressure varied from 195/120 on admission to 170/110 - 150/100. On the day of death it had risen to 200/120. He vomited frequently. Thirty-six hours after entering the hospital he had severe precordial pain; this was associated with a leathery friction rub over the heart. The venous pressure rose from 150 to 300 mm. of water. The total daily fluid intake was approximately from three to six times the urinary output. The nonprotein nitrogen decreased to 187 mg. per hundred cubic centimeters. The veins of his neck became more distended. During the last two days he was stuporous and had Cheyne-Stokes respiration. On the day of death the total urinary output was 350 cc. He had violent semiconvulsive twitching, which was controlled with difficulty by magnesium sulfate intravenously and by morphine. Death occurred on the sixth hospital day. The clinical diagnosis was chronic glomerulonephritis.

*Necropsy.*—Only the essential lesions will be discussed. There was moderate edema of the lower extremities and sacral region. The pericardial sac contained 125 cc. of clear amber colored fluid. The parietal and visceral pericardial surfaces were covered with fibrin. The heart weighed 540 Gm. The myocardium was hypertrophied; the valves and endocardium were normal.

In the ascending and transverse portions of the arch of the aorta were numerous elevated yellow intimal plaques. A few similar plaques were present in the thoracic aorta. In the abdominal aorta, in addition to a few small yellow intimal plaques, were two large areas of intimal thickening that completely surrounded and encroached on the orifices of the renal arteries and markedly reduced the size of the openings. The intimal thickening was continued for a short distance into each

renal artery. As a result of these intimal changes the orifice of the left renal artery had been reduced to a minute opening approximately 1 mm. in greatest diameter; the orifice of the right renal artery was somewhat larger, being 3 by 1 mm. in greatest diameter.

The left kidney weighed 75 Gm.; its capsule stripped with slight difficulty. A few small depressions were found on the otherwise smooth grayish yellow surface. Here and there were groups of dilated venules. The cortex varied from 6 to 8 mm. in width. The striations were not clearly defined though they did not appear irregular. The pyramids were paler than the cortex. The papillae were somewhat flattened, the calices were slightly increased in size. The pelvis and ureter were found to be normal.

The right kidney weighed 90 Gm. The capsule stripped with some difficulty. The anterior surface of this kidney resembled that of the left. The posterior surface was more irregular. At either pole and along the lateral margin it was depressed and somewhat uneven in contrast to the central elevated smooth portion. The depressed parts were grayish red and the bulging portion was yellowish gray. The cortex in the depressed areas measured 5 mm. in width and in the central elevated part 11 mm. The striations were nowhere very distinct, though not irregular. The glomeruli were vaguely seen as tiny gray dots. The pyramids were clearly defined; the papillae were somewhat flattened. The calices were slightly dilated. The pelvis and ureter were normal. The arcuate arteries in each kidney were delicate. There were a few intimal plaques in each renal artery beyond the orifice. A small aberrant artery extended into the elevated smooth portion of the right kidney.

Microscopic Examination: Since the main lesions were in the renal arteries and kidneys, the microscopic studies of these will be given in detail.

Sections of the kidneys and renal arteries were studied with a variety of stains—hematoxylin-eosin, azan carmine, elastic tissue-van Gieson and scarlet red. The intima of the renal arteries close to their orifices was thickened by a wide layer of loose meshed connective tissue whose cells were arranged parallel to the media. A few very delicate elastic fibers were found among the connective tissue cells. In the deepest part of this thickened intima of the left artery was a collection of compressed mononuclear cells and a small amount of lipid. Each intimal elastic lamella was swollen and fragmented. The media of each artery was thinner than normal; the adventitia was unaltered. The lumens of the branches of the renal arteries close to the pelvis and within the kidneys were moderately narrowed. The intima of these branches was thickened by loosely arranged fibrous tissue. Lipid was found in many of the connective tissue cells. The internal elastica was reduplicated. The media and adventitia were normal. The arterioles were not thickened, though an occasional one in the scarred areas had some lipid in its wall. No evidence of syphilitic infection was found in any of the arteries.

In both kidneys, over wide areas, glomeruli lay close together. Many of these glomeruli had thickened capsules of Bowman; in others, one or more of the capillary loops were adherent to the capsule. In many the tuft and capsule were fused together and reduced to a bloodless mass of fibrous tissue. Lipid in fine droplets was found in many of these altered glomeruli. Only rarely could tubules be identified between these damaged glomeruli. The epithelial cells of these tubules were filled with finely divided lipid. The condensed stroma in these portions of the kidneys was infiltrated with lymphocytes, and dense collections of similar cells were found at the junction of the cortex and the pyramids (fig. 1).

In the better preserved portions of the kidneys the glomeruli were somewhat larger than normal, their capillaries contained blood and the basement membrane was not thickened. The nearby tubules were moderately dilated; their epithelial cells were flat and atypical. Masses of homogeneous material resembling hemoglobin filled the lumens of many of these tubules. There was edema of the interstitial tissue but no cellular infiltration (fig. 2).

In the pyramids, some of the collecting tubules appeared normal, while others were so shrunken that no lumen could be discerned. Undoubtedly many of the collecting tubules had disappeared, as there were scattered areas in which none could be found. The epithelium of the pelvis was normal.

The central arterioles of the malpighian bodies of the spleen were sclerotic; their walls were thickened and hyalinized. The arterioles of other viscera were normal.

The anatomic diagnosis was atherosclerosis of the aorta, stenosis of the orifices of the renal arteries, atrophy of the kidneys, cardiac hypertrophy and dilatation, acute serofibrinous pericarditis, ascites, hydrothorax and edema of the legs.

## COMMENT

The case here reported was of especial interest to clinicians, particularly as regards the character of the renal lesion. Against the diagnosis of malignant hypertension were the marked albuminuria, the severe anemia and the slight arterial lesions and absence of exudate or scarring of the optic fundi. Pyelonephritis was considered an unlikely probability as there was nothing in the history to suggest a previous infection of this

Fig. 2.—Section through the better preserved portion of the right kidney. The tubules are dilated and their epithelium is flattened. The glomerulus is larger than normal. Interstitial tissue is edematous (hematoxylin-eosin stain; × 260).

type. Since the kidneys could not be palpated, renal insufficiency due to congenital polycystic disease was thought to be most unlikely. There remained for consideration chronic glomerulonephritis and, though certain of the features of the case were atypical, this was the final clinical diagnosis. The appearance of the kidneys was not suggestive of typical chronic glomerulonephritis. The broad depressed areas in the renal cortex resembled those seen in healed pyelonephritis. Against this diagnosis is the absence of any evidence of dilatation of the pelvis or ureter and of any indications of a previous or recent infection of these structures. The histologic lesions in the kidneys are obviously not those of chronic glomerulonephritis or of pyelonephritis. The absence of arteriolar sclerosis eliminates the possibility of this vascular lesion being the cause of the renal damage.

There remains for discussion the sclerosis of the renal arteries. The great reduction of the size of the orifices of these arteries must have resulted in an ischemia sufficiently marked to produce renal atrophy. The gross and histologic alterations in the kidneys are such as might be expected to follow marked ischemia. Further support for this view is afforded by the fact that the least affected portion of either kidney is that part having an additional blood supply through the aberrant artery.

630 West One Hundred and Sixty-Eighth Street.

## USE OF VITAMIN G IN PEMPHIGUS

### REPORT OF A CASE OF PEMPHIGUS VULGARIS TREATED SUCCESSFULLY WITH RIBOFLAVIN

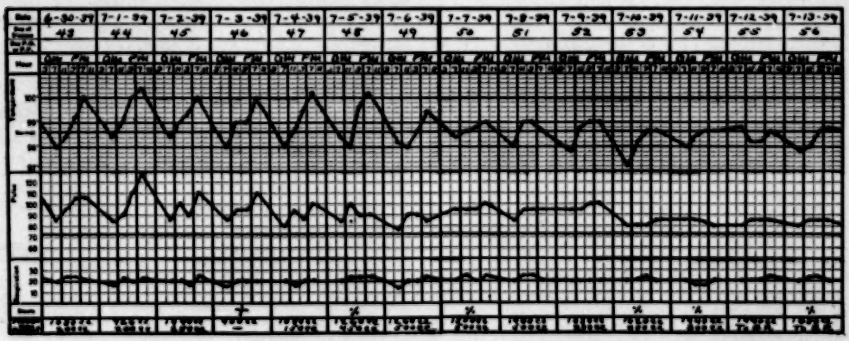
MALACHI C. TOPPING, M.D., AND AUGUST F. KNOEFEL, M.D.
TERRE HAUTE, IND.

The treatment of pemphigus has always been most unsatisfactory, as testified to by the numerous therapeutic agents in use.[1] There are two main types of pemphigus: the acute type in which death occurs in a few weeks, and the chronic type in which often there is a lapse of several years before death supervenes. The most common manifestation of the chronic type is known as pemphigus vulgaris. The use of vitamin therapy in the treatment of this disease is not without precedent. In 1932 Ludy and DeValin reported the uncomplicated recovery in six patients of pemphigus under massive dosage with viosterol. King and Hamilton[2] have also reported a case controlled by vitamin D therapy.

Many writers remark on the incidence of the disease among the lower strata of society, wherein deficiency diseases are most frequently encountered. Ludy reported that all his patients had subsisted on an unbalanced diet deficient in vitamins. A search of the literature, however, fails to reveal any one's use of vitamin G in the treatment of pemphigus. Its use in this case was on a purely experimental basis and was not predicated on known prior work except as mentioned herein.

General physical examination was essentially negative. He was muscular, of medium height and apparently well nourished. The temperature varied between 98 and 100 F., the pulse between 90 and 110. The Nikolsky sign was present. The Kahn test gave negative results. Analysis of the blood showed hemoglobin 99 per cent (15.04 Gm.), erythrocytes 4,770,000, leukocytes 10,200, polymorphonuclears 56 per cent, lymphocytes 36 per cent, monocytes 8 per cent. The Schilling count was 0-0-6-50. Urinalysis was made on a voided specimen; it was straw colored and slightly cloudy with a specific gravity of 1.024 and an acid reaction. There was no albumin, sugar or acetone present. An occasional epithelial and an occasional pus cell were reported. Blood cultures showed no growth in forty-eight hours. Fasting blood sugar was 104 mg.

Treatment was started with sulfanilamide 0.66 Gm. and sodium bicarbonate 1.33 Gm. three times a day. Continuous wet dressings of aluminum acetate solution were used on the lesions. Neoarsphenamine 0.6 Gm. was given intravenously every fourth day. June 2, fourteen days after admission, there was no indication of any improvement. The lesions present showed no evidence of healing and new lesions continued to appear. Wet dressings were discontinued and starch water and sodium bicarbonate baths were instituted three times a day. Between baths the body and sheets of the bed were freely covered with cornstarch powder. Neoarsphenamine and sulfanilamide were continued as before. June 27, thirty-nine days after admission, no change was noted. The starch water baths were of benefit in keepnig the old infected lesions free from crusts, but otherwise there was no change in his condition. The temperature chart showed a consistent evening rise in temperature to 100 or 100.2 F., the pulse rate showing a corresponding increase.




Temperature, pulse and respiratory course during hospitalization.

Our purpose in this preliminary report is not to advance or recommend its use but to report a single case in which it apparently effected a rapid and remarkable cure. The material was made by an experimental laboratory and assayed to 970 Sherman-Bourquin units per gram. It is not available for distribution, but sufficient has been made available to two dermatologic clinics for controlled use. A detailed report of their results will be published at an early date.

### REPORT OF CASE

H. W., a white man aged 51, married, a coal miner, seen May 19, 1939, complained of a generalized cutaneous eruption of four months' duration covering the entire body, including the right side of the face and the scalp. He stated that the lesions appeared as blisters and that new lesions appeared every few days. He complained also of itching and severe burning pain, associated especially with any activity or sweating. Weakness and vertigo were also present. The lesions consisted of discrete bullous areas measuring from 0.5 to 4 cm. in diameter, situated on an erythematous base. The older lesions were ruptured and in places confluent. They were weeping seropurulent exudate and were covered with incrustations.

July 7, the fiftieth day after admission, flavin concentrate 1 Gm. containing 970 Sherman-Bourquin units of vitamin G per gram was administered in orange juice and repeated daily thereafter. There was an immediate flattening of the daily temperature and pulse curves, as clearly shown in the accompanying chart. No new lesions appeared after the beginning of its administration and the old lesions, for the first time, showed definite evidence of healing. Starch baths were continued but all other medication was stopped. The patient was discharged from the hospital July 20, the sixty-third day, and has been seen at weekly intervals since. The old lesions have practically disappeared; there remain only a few erythematous and slightly pigmented areas over the back and chest. No new lesions have appeared. He makes no complaint at the present time except of weakness. His appetite is good, he sleeps well, his temperature remains normal and he has resumed all his usual activities except work in the coal mine. Resumption of this depends to some extent, perhaps, on the adjudication of his claim for workmen's compensation.

505 Tribune Building.

1. Lain, E. S., and Lamb, J. H.: Treatment of a Pemphigoid Eruption with Sulfanilamide: Report of a Case, Arch. Dermat. & Syph. 37:840 (May) 1938. Caro, M. R.: Pemphigus: Treatment with Sulfanilamide, ibid. 37:196 (Feb.) 1938. Ludy, John, and Drant, Patricia: Concerning the Treatment of Pemphigus, with Report of Cases, Urol. & Cutan. Rev. 40:105 (Feb.) 1936.

2. King, Howard, and Hamilton, C. M.: Pemphigus Controlled by Vitamin D, Arch. Dermat. & Syph. 39:515 (March) 1939.

## BILATERAL HABITUAL DISLOCATION OF THE SHOULDERS IN TWINS

### A FAMILIAL TENDENCY

PAUL B. MAGNUSON, M.D., AND JAMES K. STACK, M.D., CHICAGO

The medical literature of the past twenty-five years is replete with articles dealing with recurrent or habitual dislocation of the shoulder. The 250 or more procedures or modifications advocated for the correction of this condition attest the difficulties of finding the ideal one. Most authors stress methods of treatment, but occasionally a pedagogic outline of the subject is found in which etiology and pathology are discussed as well. The discussion of etiology usually revolves around (1) trauma and (2) "a congenital factor." There seems to be little question that severe trauma to the supporting structures of the shoulder will, in the event of improper care (or occasionally with proper care), result in a laxity which will predispose the shoulder to further dislocations. The "congenital factor," however, is referred to in a vague and cursory manner. A congenital elongation of the capsule or its muscular supports, congenital malformation of the humeral head or shallowness of the glenoid cavity are mentioned frequently but seldom with the authority of numbers or observations in the dissecting or operating room.

Such an attitude is reasonable, however, because (1) the region of the shoulder and its contiguous structures is a difficult and hazardous field in which to carry out a complete exploration and (2) most of the operations which succeed in correcting habitual dislocation are designed to obviate this necessity by plastic procedures on a remote part of the joint. A capsular plication, any variety of tendon or fascial suspension or an anterior bone block may be done in a purely mechanical way, without first finding the lesion and then correcting it, which is the usual operative procedure. A familial tendency to this vague "congenital factor" is occasionally mentioned by other authors, but we feel that it is effectively illustrated in the instance of the following cases:

### REPORT OF CASES

Ri. and Ro. K., male twins aged 19 years, white, were admitted to Passavant Memorial Hospital on Dec. 20, 1934. Each was 5 feet 5 inches (165 cm.) tall. Ri. weighed 126 pounds (57 Kg.) and Ro. 137 pounds (62 Kg.).

The relevant family history was as follows: The father, a paternal uncle and an older brother had habitual dislocations of the right shoulder. Another brother had habitual dislocations of both shoulders. Two sisters had no such difficulty but one sister "had dislocations of her knee until the age of 11." She has had none since.

Ri. stated that the first dislocation of the right shoulder occurred when he was 11 years old. It was caused by a horse stepping on his arm. No further dislocation occurred until he was 17, when the right shoulder "came out" during a football game. He was able to replace it himself, but afterward it became dislocated about once a week. The left shoulder first became involved at the age of 18 while he was playing basketball. He did not consider the injury unusual. During the following year this dislocation was repeated about eight times. He stated that the right shoulder was most easily displaced by throwing motions, while the left was displaced by blows on the arm when it was outstretched over the head.

Clinical and x-ray examination of the shoulder revealed nothing remarkable. The distance between the acromion process and the lateral condyle was the same on the two sides, as was the distance between the lateral condyle and the distal border of the palpable insertion of the pectoralis major. There was no evidence of capsular relaxation of other joints, nor had any other been dislocated.

Ro. stated that his right shoulder first became dislocated when he was 16. Since then such occurrences had been frequent. Any act in which the arm was abducted beyond the horizontal level could precipitate a dislocation. He could replace it without aid. He first dislocated the left shoulder at the age of 17 and since then had dislocated this shoulder six or seven times. On each occasion it was necessary for him to have an anesthetic before reduction could be accomplished. Here, as in the case of his brother, no clinical or x-ray changes of note could be found. In neither case was the primary trauma unduly severe.

December 21, one shoulder of each boy was operated on, a Nicola teno suspension being done. On March 10, 1935, the same procedure was carried out on the other shoulder of each patient. Two years after the second operation one shoulder of one boy again became dislocated following severe violence in the abducted and extended position. Exploration of the shoulder was carried out and no cause could be found. No recurrence has been reported since.

700 North Michigan Avenue.

These patients were referred by Dr. R. W. Doud of Normal, Ill.

From the Division of Surgery, Northwestern University Medical School.

Read before the Chicago Surgical Society, Dec. 6, 1939, and before the American College of Surgeons, sectional meeting, New Orleans, Jan. 19, 1940.

# Special Articles

## TYPHOID IN THE LARGE CITIES OF THE UNITED STATES IN 1939

### TWENTY-EIGHTH ANNUAL REPORT

As in past years, the information used in the compilation of this report was secured by addressing a communication to the health officer of each of the ninety-three cities, requesting the number of deaths from typhoid both among residents and among nonresidents which were recorded in 1939. As the population figures of the 1940 census are not yet available, the uncertainty of rates based on local estimates is recognized. In all instances the local estimate when furnished by the health officer has been used. With the approach of the new census day there are some who apparently feel that they have been unduly optimistic in claiming population increases and now submit estimates below that of 1938. The total of each of two groups of cities (South Atlantic and East North Central) is below that of last year. Probably no grave

TABLE 1.—*Death Rates of Fourteen Cities in New England States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Bridgeport | 0.0 | 0.0 | 0.0 | 0.3 | 0.5 | 2.2 | 4.8 | 5.0 | 10.3 |
| Fall River | 0.0 | 0.0 | 0.0 | 0.3* | 2.2 | 2.3 | 3.5 | 13.4 | 13.5 |
| Lynn | 0.0 | 0.0 | 0.0 | 0.2 | 1.5 | 1.6 | 3.9 | 7.2 | 14.1 |
| New Bedford | 0.0 | 0.0 | 0.0 | 1.1* | 1.5 | 1.7 | 6.0 | 15.0 | 16.1 |
| Cambridge | 0.0 | 0.0 | 0.8 | 0.9 | 2.1 | 4.3 | 2.5 | 4.0 | 9.8 |
| Lowell | 0.0 | 0.0 | 1.0 | 1.0* | 2.6 | 2.4 | 5.2 | 10.2 | 13.9 |
| Worcester | 0.0 | 0.3* | 0.3* | 0.6 | 1.0 | 2.3 | 3.5 | 5.0 | 11.8 |
| Hartford | 0.0 | 0.5* | 1.3 | 1.2 | 1.3 | 2.5 | 6.0 | 15.0 | 19.0 |
| Springfield | 0.0 | 0.7* | 0.7* | 1.0 | 0.4 | 2.0 | 4.4 | 17.6 | 19.9 |
| Waterbury | 0.0 | 0.9 | 0.0 | 0.4 | 1.2 | 1.0 | 8.0 | 18.8 | .... |
| Somerville | 0.0 | 1.0 | 0.0 | 0.4 | 1.3 | 1.6 | 2.8 | 7.9 | 12.1 |
| Providence | 0.4 | 0.0 | 0.4 | 1.1 | 1.3 | 1.8 | 3.8 | 8.7 | 21.5 |
| Boston | 0.4† | 0.6† | 0.4* | 0.6 | 1.2 | 2.2 | 2.3 | 9.0 | 16.0 |
| New Haven | 1.2† | 1.2† | 1.2 | 0.7 | 0.6 | 4.4 | 6.8 | 18.2 | 30.8 |

* All typhoid deaths were stated to be in nonresidents.

* Rate computed from population as of April 1, 1930, as no estimate for July 1, 1935, was made by the Census Bureau.

† One third or more of the reported typhoid deaths were stated to be in nonresidents.

The preceding articles in this series were published in THE JOURNAL May 31, 1913, p. 1702; May 9, 1914, p. 1473; April 17, 1915, p. 1322; April 22, 1916, p. 1305; March 17, 1917, p. 845; March 16, 1918, p. 777; April 5, 1919, p. 997; March 6, 1920, p. 672; March 26, 1921, p. 860; March 25, 1922, p. 890; March 10, 1923, p. 691; Feb. 2, 1924, p. 389; March 14, 1925, p. 813; March 27, 1926, p. 948; April 9, 1927, p. 1148; May 19, 1928, p. 1624; May 18, 1929, p. 1674; May 17, 1930, p. 1574; May 9, 1931, p. 1576; April 30, 1932, p. 1550; May 13, 1933, p. 1491; May 19, 1934, p. 1677; June 8, 1935, p. 2093; June 6, 1936, p. 1983; June 19, 1937, p. 2118; July 30, 1938, p. 414, and May 13, 1939, p. 1941.

statistical error has been committed by using the local estimate rather than falling back on the 1930 census figures. In fact, any such error is insignificant when compared with the variety of figures on typhoid deaths which are submitted (through different channels) by the same local health department or the state health department. All reallocations by place of usual residence or by source of infection are not completed at the time this report is prepared. There are some cities and states in which reallocations are apparently never prepared. There is great need of uniformity in this respect. It is expected that after the 1940 census figures become available this report can be revised, but even then it is anticipated that the corrections will be of only a minor character.

Paratyphoid has again been excluded. In tables 1 to 8 inclusive (as well as in table 10) a special note has been made of cities in which all deaths occur among nonresidents. This practice was applied first to the figures for 1937 and has been continued through 1939. Another symbol has been used to indicate those cities in which more than one third of the reported deaths were stated to have been among nonresidents.

Special attention is called to the cities listed in table 9 which report no typhoid death during the past two or more years. Bridgeport heads the list with no death in six years. Fort Wayne reports no death in five years, South Bend and Utica no death in four years, Fall River, Lynn, Milwaukee, New Bedford and Wichita no death in three years. Attention is also directed to the ten cities (Fort Worth, Scranton, Louisville, Norfolk, Canton, San Diego, Dallas, San Antonio, Camden, El Paso) which were not placed on the honor roll in table 10 merely because they have been charged with deaths among nonresidents. These cities may appropriately be considered as belonging in the honor group. Some cities are far more liberal than others in their attitude in accepting for hospitalization cases of communicable disease from the neighboring rural areas. In some instances legal circumstances compel the city to accept cases from the county.

Eleven of the large New England cities (there were only seven in 1938) report no death from typhoid in 1939 (table 1). Bridgeport has extended its good record to six years. Fall River, Lynn and New Bedford record no death in three years; Cambridge and Lowell, none in two years. Somerville, after passing through four successive years without a death, followed by one death among residents in 1938, now returns to the honor roll with no death in 1939. Springfield reports no death among residents during the past five years, Worcester none for four years, Hartford none for two years. Of three deaths reported from Boston, two occurred in nonresidents. There were only three deaths among residents in the fourteen cities in the New England states (one each in Boston, Providence, New Haven)—a truly remarkable record. The New England cities as a whole (population 2,657,824) have regained first place among the grouped cities (table 13). This enviable place was lost in 1938 to the cities of the East North Central states, which now find themselves in third place in 1939. The Middle Atlantic cities are in second place. In the New England cities there were

TABLE 2.—*Death Rates of Eighteen Cities in Middle Atlantic States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Utica | 0.0 | 0.0 | 0.0 | 0.6 | 1.1 | 3.8# | ... | ... | .... |
| Elizabeth | 0.0 | 0.0 | 0.8 | 0.9 | 1.6 | 2.4 | 3.3 | 8.0 | 16.6 |
| Syracuse | 0.0 | 0.5* | 0.0 | 0.8 | 0.8 | 2.3 | 7.7 | 12.3 | 15.6 |
| Paterson | 0.0 | 0.7 | 0.0 | 0.9 | 1.0 | 3.3 | 4.1 | 9.1 | 19.3 |
| Yonkers | 0.0 | 0.7 | 0.0 | 0.7 | 0.5 | 1.7 | 4.8 | 5.0 | 10.3 |
| Jersey City | 0.0 | 0.9 | 0.3 | 0.2 | 0.9 | 2.7 | 4.5 | 7.2 | 12.6 |
| Albany | 0.0 | 1.4 | 1.3† | 1.1 | 1.8 | 5.6 | 8.0 | 18.6 | 17.4 |
| Trenton | 0.0 | 2.4† | 0.8* | 1.1 | 2.1 | 8.2 | 8.6 | 22.3 | 28.1 |
| Buffalo | 0.2 | 0.0 | 0.2* | 0.6 | 2.7 | 3.9 | 8.1 | 15.4 | 22.6 |
| New York | 0.3 | 0.3 | 0.3 | 0.8 | 1.3 | 2.6 | 3.2 | 8.0 | 13.5 |
| Pittsburgh | 0.4† | 0.9† | 0.7† | 0.9 | 2.4 | 3.9 | 7.7 | 15.9 | 65.0 |
| Rochester | 0.6† | 0.3 | 0.0 | 0.4 | 1.7 | 2.1 | 2.9 | 9.6 | 12.8 |
| Philadelphia | 0.6† | 0.7¶ | 1.4 | 0.9 | 1.1 | 2.2 | 4.9 | 11.2 | 41.7 |
| Scranton | 0.7¶ | 0.0¶ | 0.7¶ | 1.4 | 1.8 | 2.4 | 3.8 | 9.3 | 31.5 |
| Reading | 0.9 | 0.0 | 0.0 | 0.4 | 1.6 | 6.0 | 10.0 | 31.9 | 42.0 |
| Newark | 0.9 | 0.4 | 0.0 | 0.3 | 0.9 | 2.3 | 3.3 | 6.8 | 14.6 |
| Erie | 1.6 | 0.0 | 0.8* | 1.0 | 0.9 | 2.3 | 6.9 | 49.0 | 46.6 |
| Camden | 2.5* | 1.6* | 1.6 | 2.8 | 4.4 | 5.9 | 4.9 | 4.5 | 4.0 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.
¶ Typhoid deaths furnished by Pennsylvania Department of Health, Harrisburg.

TABLE 3.—*Death Rates of Nine Cities in South Atlantic States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Wilmington | 0.0 | 2.7 | 1.8 | 1.5 | 3.1 | 4.7 | 25.8# | 23.2# | 33.0 |
| Washington | 0.6 | 1.0† | 1.9 | 2.6 | 2.8 | 5.4 | 9.5 | 17.2 | 36.7 |
| Baltimore | 0.7† | 1.5† | 1.2 | 1.4 | 3.2 | 4.0 | 11.8 | 23.7 | 35.1 |
| Norfolk | 0.8* | 0.8 | 0.8 | 4.2 | 2.2 | 2.8 | 3.5 | 21.7 | 42.1 |
| Tampa | 1.0 | 2.0† | 0.0 | 3.0 | 3.8 | 19.1 | 43.0# | ... | .... |
| Miami | 1.4 | 3.6† | 6.3 | 2.2 | 3.5 | ... | ... | ... | .... |
| Richmond | 1.6 | 2.7† | 3.2† | 2.5 | 1.9 | 5.7 | 9.7 | 15.7 | 34.0 |
| Jacksonville | 1.9 | 5.2 | 4.0 | 1.7 | 4.4 | ... | ... | ... | .... |
| Atlanta | 2.2 | 0.9† | 1.9† | 7.2 | 11.1 | 14.5 | 14.2 | 31.4 | 58.4 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 4.—*Death Rates of Eighteen Cities in East North Central States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Fort Wayne | 0.0 | 0.0 | 0.0 | 2.2 | 4.2 | 12.9 | 7.3 | ... | .... |
| South Bend | 0.0 | 0.0 | 0.0 | 0.7 | ... | ... | ... | ... | .... |
| Milwaukee | 0.0 | 0.0 | 0.0 | 0.2 | 0.8 | 1.6 | 6.5 | 13.6 | 27.0 |
| Akron | 0.0 | 0.4 | 1.0† | 0.6 | 1.5 | 2.4 | 10.6 | 21.0 | 27.7# |
| Evansville | 0.0 | 0.9* | 2.7† | 1.9 | 6.3 | 5.0 | 17.5 | 32.0 | 35.0 |
| Flint | 0.0 | 1.2 | 3.0† | 0.7 | 1.6 | 4.6 | 22.7 | 18.8 | 46.9 |
| Dayton | 0.0 | 1.3† | 1.4† | 0.8 | 1.9 | 3.3 | 9.3 | 14.8 | 22.5 |
| Chicago | 0.3 | 0.3 | 0.3 | 0.4 | 0.6 | 1.4 | 2.4 | 8.2 | 15.8 |
| Toledo | 0.3 | 0.3* | 1.2* | 1.3 | 3.0 | 5.8 | 10.6 | 31.4 | 37.5 |
| Detroit | 0.5 | 0.2† | 0.3 | 0.6 | 1.5 | 4.1 | 8.1 | 15.4 | 22.8 |
| Cleveland | 0.5† | 0.3† | 0.5 | 1.1 | 1.0 | 2.0 | 4.0 | 10.0 | 15.7 |
| Grand Rapids | 0.6 | 0.0 | 1.6* | 0.2 | 1.0 | 1.9 | 9.1 | 25.5 | 29.7 |
| Canton | 0.9* | 0.0 | 0.0 | 0.9 | 1.4 | 3.3 | 8.9 | ... | .... |
| Columbus | 0.9† | 0.3 | 1.5 | 2.0 | 2.1 | 3.5 | 7.1 | 15.9 | 40.0 |
| Cincinnati | 1.0† | 0.6 | 1.3† | 1.4 | 2.5 | 3.2 | 3.4 | 7.8 | 30.1 |
| Youngstown | 1.1 | 0.0 | 1.1 | 1.1 | 1.1 | 7.2 | 19.2 | 29.5 | 35.1 |
| Peoria | 1.6 | 0.0 | 1.7* | 0.9 | 0.2 | 3.7 | 5.7 | 16.4 | 15.7# |
| Indianapolis | 1.9† | 1.3 | 1.3 | 1.2 | 2.7 | 4.6 | 10.3 | 20.5 | 30.4 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 5.—*Death Rates of Six Cities in East South Central States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Chattanooga | 0.0 | 1.7 | 1.7 | 4.7 | 8.0 | 18.6 | 27.2 | 35.8# | .... |
| Louisville | 0.5* | 0.8† | 0.6* | 2.3 | 3.7 | 4.9 | 9.7 | 19.7 | 52.7 |
| Birmingham | 1.0† | 1.7† | 1.4 | 3.9 | 8.0 | 10.8 | 31.5 | 41.3 | 41.7 |
| Nashville | 3.0† | 4.9† | 1.2* | 5.6 | 18.2 | 17.8 | 20.7 | 40.2 | 61.3 |
| Knoxville | 3.8 | 3.9 | 3.2 | 5.7 | 10.7 | 20.8 | 25.3# | ... | .... |
| Memphis | 5.7† | 3.1† | 4.9† | 7.9 | 9.3 | 18.9 | 27.7 | 42.5 | 35.3 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

recorded six deaths in 1939, only one half the number for 1938 and 1937.

The Middle Atlantic states (table 2) have a group rate (0.37) which is lower than that of 1938 (0.44) and 1937 (0.51). There has been no death recorded in Utica for the past four years, none in Elizabeth for two years. Eight cities (Utica, Elizabeth, Syracuse, Paterson, Yonkers, Jersey City, Albany, Trenton) report no typhoid death in 1939. There were six such cities in 1938, seven in 1937. Scranton records no death among residents during the past six years, Camden none for two years. Buffalo, after two years with no death among residents, reports one such death in 1939; Erie, after no death among residents in four years, reports two such deaths in 1939. Newark records the highest incidence of typhoid in twelve years (twenty-five cases) and the largest number of deaths in seven

TABLE 6.—*Death Rates of Nine Cities in West North Central States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Wichita | 0.0 | 0.0 | 0.0 | 0.7 | 1.2 | 6.3 | ... | .... | .... |
| Kansas City, Kan. | 0.0 | 0.0 | 0.8* | 1.1 | 1.7 | 5.0 | 9.4 | 31.1 | 74.3# |
| St. Paul | 0.0 | 0.7 | 0.0 | 0.7 | 1.4 | 3.4 | 3.1 | 9.2 | 12.8 |
| Duluth | 0.0 | 1.0 | 0.0 | 1.0 | 1.1 | 1.7 | 4.4 | 19.6 | 45.5 |
| Minneapolis | 0.2 | 0.0 | 0.2* | 0.8 | 0.8 | 1.9 | 5.0 | 10.6 | 32.1 |
| Omaha | 0.4 | 0.0 | 1.3 | 0.9 | 1.3 | 3.3 | 5.7 | 14.9 | 40.7 |
| St. Louis | 0.7† | 0.5 | 1.1† | 1.6 | 2.1 | 3.9 | 6.5 | 12.1 | 14.7 |
| Kansas City, Mo. | 0.9 | 0.7† | 1.4† | 1.5 | 2.8 | 5.7 | 10.6 | 16.2 | 35.6 |
| Des Moines | 1.3 | 0.7 | 0.7 | 2.1 | 2.4 | 2.2 | 6.4 | 15.9 | 23.7 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

TABLE 7.—*Death Rates of Eight Cities in West South Central States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Fort Worth | 0.5* | 2.7† | 2.2 | 4.6 | 5.9 | 6.1 | 16.3# | 11.9 | 27.8 |
| Tulsa | 1.3 | 0.6 | 0.0 | 1.1 | 6.3 | 16.3# | ... | ... | .... |
| Houston | 1.6† | 3.1 | 2.0 | 3.2 | 4.8 | 7.6 | 14.2 | 38.1 | 49.3# |
| Dallas | 1.6* | 4.3† | 3.6* | 5.4 | 7.3 | 11.2 | 17.2 | .... | .... |
| San Antonio | 2.3* | 2.3† | 3.8 | 4.2 | 4.6 | 9.3 | 23.3 | 29.5 | 35.9 |
| Oklahoma City | 2.7 | 1.3 | 3.1 | 4.3 | 7.4# | ... | ... | ... | .... |
| El Paso | 5.6* | 5.9 | 0.0 | 4.9 | 9.1 | 10.4 | 28.7 | 42.6 | .... |
| New Orleans | 6.9† | 5.5† | 2.3† | 9.6 | 9.9 | 11.6 | 17.5 | 29.9 | 35.6 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

years (seven deaths). It is stated that practically all of the cases were due to contact with a mild case acting as a carrier. New York reports twenty-two deaths (the same number as in 1938), of which twenty (as in 1938) were among residents. Philadelphia reports twelve deaths (fifteen in 1938), six among residents. Pittsburgh reports three deaths, two among nonresidents. After two years with no death, Reading reports one death among residents. The health officer of Scranton records no typhoid death; however, the Pennsylvania Department of Health has charged one death to this city. Syracuse reports no death among residents during the past four years. In the group as a whole (population 13,602,500) there were fifty-one deaths in 1939 compared with fifty-nine in the preceding year. There was but one geographic area which had a lower death rate for 1939, the New England.

The rate (table 3) for the South Atlantic cities (1.03) is much improved over the rates of 1938 (1.74) and 1937 (1.96) and is considerably lower than that of 1936 (1.55). It is but slightly more than a third the rate for the quinquennial period 1931-1935 (2.70). In these cities (population 2,622,237) there occurred twenty-seven deaths in 1939 and forty-six in 1938. There was but one city (Wilmington) without a death in 1938, although Norfolk recorded its one death among nonresidents. Nine (one third) of the deaths

TABLE 8.—*Death Rates of Eleven Cities in Mountain and Pacific States from Typhoid per Hundred Thousand of Population*

| | 1939 | 1938 | 1937 | 1931-1935 | 1926-1930 | 1921-1925 | 1916-1920 | 1911-1915 | 1906-1910 |
|---|---|---|---|---|---|---|---|---|---|
| Salt Lake City | 0.0 | 0.0 | 0.7 | 1.0 | 1.9 | 4.0 | 9.3 | 13.2 | 41.1 |
| San Francisco | 0.0 | 0.7 | 0.6 | 0.8 | 2.0 | 2.8 | 4.6 | 13.6 | 36.3 |
| Seattle | 0.3 | 0.0 | 0.0 | 0.6 | 2.2 | 2.6 | 2.9 | 5.7 | 25.2 |
| Portland | 0.3 | 0.0 | 0.3 | 0.6 | 2.3 | 3.5 | 4.5 | 10.8 | 23.2 |
| Oakland | 0.5 | 0.0† | 0.3 | 1.0 | 1.2 | 2.0 | 3.8 | 8.7 | 21.5 |
| Los Angeles | 0.4 | 0.0† | 0.7† | 0.8 | 1.5 | 3.0 | 3.6 | 10.7 | 19.0 |
| Long Beach | 0.6 | 0.6 | 0.0 | 0.2 | 1.1 | 2.1# | ... | ... | .... |
| Tacoma | 0.9 | 0.0 | 0.0 | 0.7 | 1.8 | 3.7 | 2.9 | 10.4 | 19.0 |
| San Diego | 1.0* | 0.0 | 1.0† | 1.3 | 1.0 | 1.6 | 7.9 | 17.0 | 10.8 |
| Denver | 1.9 | 1.9 | 2.7 | 1.8 | 2.6 | 5.1 | 5.8 | 12.0 | 37.5 |
| Spokane | 2.4† | 2.4† | 0.0 | 1.4 | 2.2 | 4.4 | 4.9 | 17.1 | 20.3 |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.
# Incomplete data.

in the group of cities as a whole occurred among nonresidents. The percentage of deaths among nonresidents is less significant than for former years. Of seven deaths recorded for Atlanta, two were among nonresidents; of four in Washington, one was among nonresidents. Baltimore records but one death among residents (five among nonresidents). The health officer states that only twenty-four cases (less than half of any previous year) were reported in Baltimore. The three deaths in Richmond, three in Jacksonville, two in Miami and one in Tampa occurred in residents.

The East North Central cities (population 9,883,376) experienced a setback and dropped from first place in 1938 to third in 1939 (table 4). The number of typhoid deaths increased from thirty-five to forty-four (the rate from 0.35 to 0.44). The rate remains, however, below that of 1937 (0.62) and of the quinquennial period 1931-1935 (0.75). As in 1938 there are seven cities (Fort Wayne, South Bend, Milwaukee, Akron, Evansville, Flint, Dayton) which report no death in 1939. They are not, however, altogether the same cities. Grand Rapids with one death among residents in 1939, Canton with one among nonresidents, Youngstown and Peoria each with two deaths among residents, have been

TABLE 9.—*Fourteen Cities with No Typhoid Death in 1938 and 1939*

| | | |
|---|---|---|
| Bridgeport * | Kansas City, Kan. | Salt Lake City |
| Cambridge | Lowell | South Bend ¶ |
| Elizabeth | Lynn † | Utica ¶ |
| Fall River † | Milwaukee † | Wichita † |
| Fort Wayne ** | New Bedford † | |

* No typhoid death in six years.
** No typhoid death in five years.
¶ No typhoid death in four years.
† No typhoid death in three years.

dropped from the honor list. There are four cities (Cleveland, Columbus, Cincinnati, Indianapolis) in which one third or more of the reported deaths were stated to be among nonresidents. Fort Wayne reports no typhoid death in five years, South Bend no death in four years, Milwaukee no death in three years. Chicago reports nine deaths, all among residents. Of five deaths each in Cincinnati and Cleveland, two were among nonresidents. Of eight deaths in Detroit, one was among nonresidents. The health officer reports that, of twenty-

six cases, nine obtained their infection while out of the city, five were infected by contact with typhoid carriers, one was reallocated to Detroit from a neighboring township, and in eleven instances the source of infection could not be ascertained.

TABLE 10.—*Death Rates from Typhoid in 1939*

| Honor Roll: No Typhoid Deaths (Thirty-Four Cities) | | |
|---|---|---|
| Akron | Fort Wayne | South Bend |
| Albany | Hartford | Springfield |
| Bridgeport | Jersey City | St. Paul |
| Cambridge | Kansas City, Kan. | Syracuse |
| Chattanooga | Lowell | Trenton |
| Dayton | Lynn | Utica |
| Duluth | Milwaukee | Waterbury |
| Elizabeth | New Bedford | Wichita |
| Evansville | Paterson | Wilmington |
| Fall River | Salt Lake City | Worcester |
| Flint | San Francisco | Yonkers |
| | Somerville | |

| First Rank: from 0.1 to 1.9 Deaths per Hundred Thousand (Forty-Nine Cities) | | | | | |
|---|---|---|---|---|---|
| Buffalo | 0.2 | Grand Rapids | 0.6 | Cincinnati | 1.0† |
| Minneapolis | 0.2 | Long Beach | 0.6 | San Diego | 1.0* |
| Chicago | 0.3 | Philadelphia | 0.6† | Tampa | 1.0 |
| New York | 0.3 | Rochester | 0.6† | Youngstown | 1.1 |
| Oakland | 0.3 | Washington | 0.6 | New Haven | 1.2† |
| Portland | 0.3 | Baltimore | 0.7† | Des Moines | 1.3 |
| Seattle | 0.3 | Scranton | 0.7* | Tulsa | 1.3 |
| Toledo | 0.3 | St. Louis | 0.7† | Miami | 1.4 |
| Boston | 0.4† | Louisville | 0.8* | Dallas | 1.6* |
| Los Angeles | 0.4 | Norfolk | 0.8* | Erie | 1.6 |
| Omaha | 0.4 | Canton | 0.9* | Houston | 1.6† |
| Pittsburgh | 0.4† | Columbus | 0.9† | Peoria | 1.6 |
| Providence | 0.4 | Kansas City, Mo. | 0.9 | Richmond | 1.6 |
| Cleveland | 0.5† | Newark | 0.9 | Denver | 1.9 |
| Detroit | 0.5 | Reading | 0.9 | Indianapolis | 1.9† |
| Fort Worth | 0.5* | Tacoma | 0.9 | Jacksonville | 1.9 |
| | | Birmingham | 1.0† | | |

| Second Rank: from 2.0 to 4.9 (Seven Cities) | | | | | |
|---|---|---|---|---|---|
| Atlanta | 2.2 | Spokane | 2.4† | Nashville | 3.0† |
| San Antonio | 2.3* | Camden | 2.5* | Knoxville | 3.8 |
| | | Oklahoma City | 2.7 | | |

| Third Rank: from 5.0 to 6.9 (Three Cities) | | | | | |
|---|---|---|---|---|---|
| El Paso | 5.6* | Memphis | 5.7† | New Orleans | 6.9† |

* All typhoid deaths were stated to be in nonresidents.
† One third or more of the reported typhoid deaths were stated to be in nonresidents.

The six cities (table 5) in the East South Central group (population 1,364,025) again show an increase in the death rate (2.42 in 1939, 2.36 in 1938, 2.10 in 1937). The rate remains far below that of 1936 (3.35)

TABLE 11.—*Number of Cities with Various Typhoid Death Rates*

| | No. of Cities | 10.0 and Over | 5.0 to 9.9 | 2.0 to 4.9 | 1.0 to 1.9 | 0.1 to 0.9 | 0.0 |
|---|---|---|---|---|---|---|---|
| 1906-1910 | 77 | 75 | 2 | 0 | 0 | 0 | 0 |
| 1911-1915 | 79 | 50 | 19 | 2 | 0 | 0 | 0 |
| 1916-1920 | 84 | 22 | 32 | 30 | 0 | 0 | 0 |
| 1921-1925 | 89 | 12 | 17 | 44 | 12 | 0 | 0 |
| 1926-1930 | 92 | 3 | 10 | 30 | 37 | 12 | 0 |
| 1931-1935 | 93 | 0 | 6 | 17 | 28 | 42 | 0 |
| 1930 | 93 | 2 | 6 | 30 | 23 | 22 | 10 |
| 1931 | 93 | 2 | 6 | 23 | 28 | 22 | 12 |
| 1932 | 93 | 1 | 7 | 13 | 29 | 29 | 14 |
| 1933 | 93 | 0 | 7 | 14 | 19 | 33 | 20 |
| 1934 | 93 | 0 | 9 | 11 | 27 | 23 | 23 |
| 1935 | 93 | 0 | 7 | 15 | 18 | 29 | 24 |
| 1936 | 93 | 0 | 3 | 15 | 21 | 30 | 24 |
| 1937 | 93 | 0 | 1 | 13 | 26 | 26 | 27 |
| 1938 | 93 | 0 | 2 | 13 | 14 | 34 | 29 |
| 1939 | 93 | 0 | 3 | 7 | 17 | 32 | 34 |

and that of the quinquennial period 1931-1935 (4.81). The actual number of deaths in these six cities increased but one, from thirty-two in 1938 to thirty-three in 1939. For the first time, one of these cities (Chattanooga) is included in the list of those cities without a death in 1939. In addition to this there are three cities (Birmingham, Nashville, Memphis) in which one third or more of the reported deaths were stated to be among nonresidents. It is here evident that the surrounding rural areas continue to contribute to the hospital load and thus to the death rate of these urban centers. Birmingham, with three deaths, reports one among nonresidents; Nashville, with five deaths, records four in nonresidents; Memphis, with seventeen deaths, reports twelve in nonresidents. The health officer of Memphis reports twenty-eight cases in residents: six among white persons, twenty-two among Negroes. The attack rate for Negroes is nearly six times that of the white population. Since Memphis serves as a hospital center for the surrounding territory, thirty-six additional cases were brought into the city for treatment (thirteen white with five deaths, twenty-three Negroes with seven

TABLE 12.—*Total Typhoid Rate for Seventy-Eight Cities 1910-1939* *

| | Population | Typhoid Deaths | Typhoid Death Rate per 100,000 |
|---|---|---|---|
| 1910 | 22,573,435 | 4,637 | 20.54 |
| 1911 | 23,211,341 | 3,959 | 17.06 |
| 1912 | 23,835,309 | 3,132 | 13.14 |
| 1913 | 24,457,989 | 3,295 | 13.43 |
| 1914 | 25,091,112 | 2,761 | 11.00 |
| 1915 | 25,713,346 | 2,434 | 9.47 |
| 1916 | 26,357,550 | 2,191 | 8.34 |
| 1917 | 26,885,498 | 2,016 | 7.50 |
| 1918 | 27,086,026† | 1,824† | 6.73 |
| 1919 | 27,735,063† | 1,151† | 4.15 |
| 1920 | 28,244,878 | 1,088 | 3.85 |
| 1921 | 28,859,002 | 1,141 | 3.95 |
| 1922 | 29,473,246 | 983 | 3.33 |
| 1923 | 30,087,439 | 959 | 3.18 |
| 1924 | 30,701,614 | 945 | 3.07 |
| 1925 | 31,315,596 | 1,079 | 3.44 |
| 1926 | 31,929,782 | 907 | 2.84 |
| 1927 | 32,543,986 | 648 | 1.99 |
| 1928 | 33,158,150 | 629 | 1.89 |
| 1929 | 33,772,334 | 537 | 1.59 |
| 1930 | 34,386,717 | 554 | 1.61 |
| 1931 | 35,137,915 | 563 | 1.60 |
| 1932 | 35,691,815 | 442 | 1.24 |
| 1933 | 35,691,815 | 423 | 1.18 |
| 1934 | 35,691,715 | 413 | 1.17 |
| 1935 | 35,691,715 | 348 | 0.98‡ |
| 1936 | 36,716,404 | 336 | 0.93§ |
| 1937 | 36,771,787 | 280 | 0.76‖ |
| 1938 | 36,972,985 | 248 | 0.67‖ |
| 1939 | 37,112,005 | 229 | 0.62‖# |

* The following fifteen cities are omitted from this table because data for the full period are not available: Canton, Chattanooga, Dallas, Fort Wayne, Jacksonville, Knoxville, Long Beach, Miami, Oklahoma City, South Bend, Tampa, Tulsa, Utica, Wichita, Wilmington.
† Data for Fort Worth lacking.
‡ The rate for ninety-three cities in 1935 was 1.03 (total population 37,437,812, typhoid deaths 385), whereas in 1930 it was 1.64 and in 1933 and 1934 it was 1.24 and 1.25 respectively. The 1931-1935 average for the ninety-three cities is 1.31.
§ Rate for ninety-three cities in 1936 was 0.96 (total population 38,249,694, typhoid deaths 365).
‖ Rate for ninety-three cities in 1937 was 0.82 (total population 38,885,435, typhoid deaths 318).
# Rate for ninety-three cities in 1938 was 0.74 (total population 39,143,556, typhoid deaths 291).
‖‖ Rate for ninety-three cities in 1939 was 0.67 (total population 39,354,549, typhoid deaths 265).
Special Note:—Deaths for 1936 have been corrected, as Yonkers originally reported seven deaths and later corrected report to one death.

deaths). As one third of the nonresident patients died, it is fair to conclude that only the unfavorable cases were hospitalized, the milder cases not being sent to Memphis. Knoxville records five deaths, four among residents. Louisville deserves special mention as all three deaths were among nonresidents.

The West North Central group (table 6) (population 2,809,679) shows an increase in the death rate (0.50 in 1939, 0.40 in 1938). In second place in 1938, this group in 1939 just edges out the Mountain and Pacific group for fourth place. The increase in the number of deaths is but three (from eleven in 1938 to fourteen in 1939). As in 1938 there are four cities (Wichita, Kansas City, Kan., St. Paul, Duluth) which report no death in 1939. They are not, however, altogether the same cities. Minneapolis and Omaha, each with one death among residents, have been dropped from the honor list. Minneapolis had reported no death

among residents for three years prior to 1939. Duluth returns to the honor roll after an absence of one year (no deaths in 1936 and 1937). Only one death has occurred in Duluth during the past four years. In 1938 this was the only group in which there was no city with a death rate in excess of 1.0. In 1939 there is no such group, although the West North Central cities maintain second place (Des Moines with 1.3) while the

TABLE 13.—*Total Typhoid Death Rate per Hundred Thousand of Population for Ninety-Three Cities According to Geographic Divisions*

| | Population | Typhoid Deaths | | Typhoid Death Rates | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1931-1935 | 1926-1935 |
| New England | 2,857,624 | 6 | 12 | 0.23 | 0.45 | 0.45 | 0.70 | 1.31 |
| Middle Atlantic | 13,682,580 | 51 | 59 | 0.37 | 0.44 | 0.51 | 0.80 | 1.40 |
| South Atlantic | 2,822,237 | 27 | 46 | 1.03 | 1.74 | 1.98 | 2.70 | 4.50 |
| East North Central | 9,883,376 | 44 | 35 | 0.44 | 0.35 | 0.62 | 0.75 | 1.39† |
| East South Central | 1,364,625 | 35 | 32 | 2.42 | 2.36 | 2.10 | 4.61 | 8.31 |
| West North Central | 2,689,679 | 14 | 11 | 0.50 | 0.40 | 0.76 | 1.34 | 1.83 |
| West South Central | 2,138,496 | 68 | 74 | 3.19 | 3.52 | 2.34 | 5.38 | 7.32‡ |
| Mountain and Pacific | 4,276,412 | 22 | 22 | 0.51 | 0.52 | 0.68 | 0.98 | 1.80 |

† Data for South Bend for 1925-1929 are not available.
‡ Lacks data for Oklahoma City in 1926.

New England cities take first place (New Haven with 1.2). Kansas City, Kan., reports no death among residents for the past three years, while Wichita records no death either among residents or nonresidents for three years. Of six deaths in St. Louis and four in Kansas City, Mo., three each were among residents.

The eight cities of the West South Central group (table 7) (population 2,138,496) report a reduction in the death rate (3.52 in 1938, 3.19 in 1939). The actual number of deaths decreased from seventy-four to sixty-eight. Special mention should be made of El Paso and San Antonio, each reporting six deaths, all among nonresidents; Dallas recording five deaths and Fort Worth one death, all among nonresidents. New Orleans reports thirty-six deaths, twenty-four among nonresidents. Excluding New Orleans, there were thirty-two deaths reported by the cities in this group, of which twenty-one, or two thirds, were among nonresidents. Houston reports six deaths, three among residents; Oklahoma City six, all among residents.

The cities in the Mountain and Pacific states (table 8) report the same number of deaths as in 1938 (twenty-two) and consequently but a slight reduction in the rate (0.51 in 1939, 0.52 in 1938). While in 1938 there were five cities with no death, in 1939 there were but two (Salt Lake City, San Francisco) such cities and only Salt Lake City appears on the honor roll for the two years. San Diego with no death in 1938 and two deaths among nonresidents in 1939 deserves special mention. Tacoma, Portland and Seattle, each with one resident death, have been dropped from the honor roll. Spokane records three deaths, two among residents. Denver reports six deaths among residents and does not keep a record of deaths among nonresidents. Los Angeles records six deaths, five among residents. In October 1939 thirty-five cases in the city and ten additional cases in the county were caused by a carrier who contaminated chocolate éclairs.

### THE HONOR ROLL

The number of cities with no death from typhoid has increased to thirty-four. In 1936 there were but eighteen such cities, in 1937 twenty-seven, in 1938 twenty-nine. Of particular significance are the data in table 9, which furnishes the names of fourteen cities with no typhoid death in 1938 and 1939. Several cities have continued their excellent records. We again find (as in 1938) three cities in the third rank (table 10). It should be emphasized, however, that in El Paso all deaths were stated to be in nonresidents and in Memphis twelve of seventeen deaths were in nonresidents. As repeatedly stated, several other cities in the first and second rank would appear in the honor roll were they not charged with deaths in nonresidents. Table 11 continues to show a definite swing "to the right" with a marked reduction in the number of cities with a rate of 2.0 and above.

For the seventy-eight cities (table 12) for which data are available since 1910, there occurred 239 deaths from typhoid in 1938, which is the lowest of record (248 in 1938, 280 in 1937). The rate for this group of cities is for the fifth consecutive year less than 1.0. The rate for the ninety-three cities studied in 1939 is also below 1.0 (0.67) and below the corresponding rate for 1937 (0.74). This annual review again shows a downward trend in the death rate from typhoid in the large cities of the United States. No outbreak of epidemic proportion has been recorded in these cities. Routine vaccination of the population is not practiced except under flood conditions. In progressive communities vaccination is urged for contacts to cases and for persons who travel widely in countries where sanitary conditions are not of the best. Noteworthy gains have been made throughout the country. The New England and Middle Atlantic groups have maintained their excellent rates of many years' standing.

---

## OVARIAN HORMONES AND FEMALE GENITAL CANCER

EDGAR ALLEN, PH.D.
Professor of Anatomy, Yale University School of Medicine
NEW HAVEN, CONN.

This paper does not attempt to summarize even the most recent work in this field. Instead, it merely outlines the development of my own point of view on the subject from the early work on the follicular hormone in which normal reactions were reproduced to work of more recent date indicating a possible role of this hormone in mammary and uterine cancer. Since the early work with Dr. Doisy on this hormone was done in St. Louis at Washington University School of Medicine, it means a great deal to me now [1] to be able to present some more recent studies which have led to the experimental production of genital cancer.

I intend first to summarize briefly some of the principal results obtained in studies of animal reactions to ovarian hormones, especially estrogenic hormone, emphasizing above all its effect of producing growth in the female genital organs, for it seems to me that estrogenic hormone above all else is a growth hormone, concentrating its action on the female genital organs.

In the normal animal, after this genital growth hormone has been acting for a while, the genital tissues are raised to a high plane of function, which is usually rather transitory. Then there is a phase of retrogression, especially in the vagina and uterus and to some

The first Barnard Hospital Lecture, read before the St. Louis Medical Society, Oct. 31, 1939.

1. It is a special honor to be invited to give this first Barnard Hospital Lecture, inaugurated under Dr. E. V. Cowdry's directorship of research in this hospital. Contacts with him and with three of his predecessors, Dr. Leo Loeb, Dr. Montrose T. Burrows and Dr. George M. Smith, have contributed a great deal to the development of the point of view expressed herein.

extent also in the mammary glands. In some animals a period of rest intervenes before the estrogenic hormone again reaches a concentration high enough to start another phase of growth in the genital organs.

After summarizing some of the effects of estrogens in experimental animals when the hormone is given in small doses over short periods, attention will be focused on what can be done by long continued treatment with this growth producing hormone in high doses.[2] In other words, instead of permitting the genital organs to regress and rest briefly after short phases of growth and function, the experiments attempt to keep them growing more or less continuously over long periods. Under such conditions it is possible to produce quite abnormal growths—decidedly atypical growths—and in some cases cancer follows.[3]

Of course, there may be many etiologic factors in cancer other than hormonal stimulation: genetic, traumatic, chemical, parasitic, and even bacteria, viruses and other factors. Obviously hormonal stimulation is only one of several factors in the etiology of female genital cancer.

## A BEGINNING

Because this paper is to sketch my own point of view on this subject, I wish to mention briefly the background. After two years in the army, with graduate work toward a Ph.D. degree incomplete, and never having been farther west than Buffalo, I came to St. Louis in the fall of 1919. My start was as instructor in anatomy in Dr. Terry's department at Washington University School of Medicine. As training for this job of teaching and investigation in a medical school I had had only preparation in zoology.

It was necessary for me to get started on a doctor's thesis. I had been most interested in embryology—in reproduction. No one had succeeded in attempts to fertilize mammalian eggs in vitro. This still seems to me a most interesting problem.

Dr. Charles H. Danforth, now professor of anatomy at Stanford University School of Medicine, had a colony of mice on which he was studying the inheritance of such characteristics as a hereditary anemia present before birth, hereditary obesity peculiar to yellow mice, and other things. This was my introduction to inbred strains of mice as experimental animals *par excellence*.

Seven months of attempting to fertilize mouse eggs yielded only failure. In attempts to get the eggs it was necessary to learn something about the nonpregnant sexual cycle. When the first objective (fertilization in vitro) failed, the estrous cycle became the subject of my thesis, and this led directly to my early work with Dr. Doisy and others on the ovarian follicular hormone.

The problem considered in the thesis was strictly morphologic. The ovary and genital tract were studied microscopically and an attempt was made to explain function by correlating the results.[4] It was observational. There was no experimental work involved. At that time most statements concerning the internal secretions of the ovaries stressed the corpora lutea as the endocrine glands of the ovary. Clinical books especially, with their emphasis on implantation, seldom mentioned the follicles as possible endocrine structures. Leo Loeb[5] and Stockard and Papanicolaou,[6] working with the guinea pig, and Long and Evans,[7] working with the rat, had recognized the importance of the follicles in hormone secretion, but their work, like mine with the mouse, was mostly observational and did not include experimental tests of ovarian extracts.

The point that impressed me most strongly from the work on the mouse was that there might be a succession of nonpregnant cycles without ovulation and consequently without the formation of corpora lutea; in other words, that the follicular hormone alone should be sufficient to explain the succession of cyclic phenomena in the nonpregnant uterus and vagina. This focused my attention on the liquor folliculi as a source of this hormone.

At that time the discovery by Banting and Best of insulin had just made investigators hormone conscious, and Drs. Shaffer and Doisy were working intensively on insulin. Dr. Doisy undertook the chemical fractionation of follicular fluid. It is fun now to recall picking over ovaries from a bucket in the meat packing plant, my wife and I aspirating the fluid from the follicles on the kitchen table at home, Dr. Doisy beginning his extraction of the active fraction and our early tests of follicular hormone on mice. One of the remarkable things about that first experiment was that all the animals injected gave positive reactions.[8]

*Growth in Female Genital Organs Produced by Estrogens.*—Even in those first experiments it was clear that the outstanding effect of this hormone was to produce growth in the female genital organs. This was clearly shown by the vaginal reaction, in which growth in forty-eight hours thickens the vaginal wall of the castrate rodent from two or three layers to more than a dozen layers.[9] In most instances the treatment was of short duration and the dosages were very small. In the first years of work with this hormone, concentrated extracts were not available. Later crystallization[10] and then synthesis[11] of estrogens was accomplished. More than forty substances are now available for which estrogenic activity has been demonstrated.

*Estrous Cycles, Successive Waves of Growth.*—One of the points which seemed to me most important in the reaction of rodents to injected estrogen was that experimental estrous cycles could be produced by the injection of this follicular hormone. This must mean that, fundamentally, the normal nonpregnant cycle in the vagina and uterus of the mouse was merely a succession of waves of growth, at the peak of which would occur short periods of function and which would be followed by periods of retrogression. In fact, in the normal mouse and rat there is no luteal phase of the cycle unless the animal is mated. It requires cervical stimulation to activate the corpora lutea. So, as far as the nonpregnant cycle in these animals is concerned,

2. The lecture was illustrated by lantern slides, which made a detailed description of the effects of the hormone unnecessary.

3. Allen, Edgar; Hisaw, F. L., and Gardner, W. U.: Endocrine Functions of the Ovaries, chapter X in Sex and Internal Secretions, ed. 2, edited by Edgar Allen, C. H. Danforth and E. A. Doisy. Baltimore, Williams & Wilkins Company, 1939. Many references are cited here.

4. Allen, Edgar: The Estrous Cycle in the Mouse, Am. J. Anat. **30**: 297 (May) 1922.

5. Loeb, Leo: The Relation of the Ovary to the Uterus and the Mammary Gland from the Experimental Aspect, Surg., Gynec. & Obst. **25**: 300 (Sept.) 1917; Am. J. Obst. **76**: 681, 1919.

6. Stockard, C. R., and Papanicolaou, G. N.: The Existence of a Typical Estrous Cycle in the Guinea Pig, with a Study of Its Histological and Physiological Changes, Am. J. Anat. **22**: 225 (Sept.) 1917.

7. Long, J. A., and Evans, H. M.: The Estrous Cycle in the Rat and Its Associated Phenomena, Mem. Univ. California **6**: 1, 1922.

8. Allen, Edgar, and Doisy, E. A.: An Ovarian Hormone: A Preliminary Report on Its Localization, Extraction and Partial Purification, and Action in Test Animals, J. A. M. A. **81**: 819 (Sept. 8) 1923.

9. Allen, Edgar; Doisy, E. A.; Francis, B. F.; Gibson, H. V.; Robertson, L. L.; Colgate, C. E.; Kountz, W. B., and Johnston, C. G.: Hormone of the Ovarian Follicle: Its Localization and Action in Test Animals and Additional Points Bearing upon the Internal Secretion of the Ovary, Am. J. Anat. **34**: 133 (Sept.) 1924.

10. Doisy, E. A.; Veler, E. D., and Thayer, S.: Folliculin from the Urine of Pregnant Women, Am. J. Physiol. **90**: 329, 1929.

11. Marker, R. E.; Kamm, O.; Oakwood, T. S., and Laucius, J. F.: Synthetic Preparation of Estrone (Theelin), J. Am. Chem. Soc. **58**: 1503, 1936.

the corpora lutea are not important. It should be noted that this refers to the nonpregnant cycle. When this statement was made in a paper presented at the Washington University Medical Society, the comment by a prominent clinician was that, while this might be true in the mouse and rat, it certainly didn't apply to the menstrual cycle in women.

*Experimental Menstrual Cycles.*—This comment led to attempts to produce experimentally menstrual cycles in monkeys. The first work was begun here during the summer of 1923. Later it was possible to establish a colony of monkeys at the University of Missouri and repeat on monkeys this work begun on rodents. The first menstrual cycles experimentally induced by injections of ovarian hormone were completed in castrate monkeys [12] in 1927. It was six years later (1933) that Werner and Collier [13] at St. Louis University School of Medicine produced the first experimental menstruation in ovariectomized women with theelin. Six years was a long time to wait for confirmation in women of experimental menstruation. At that time the accepted explanation of menstruation was that menses followed cessation of function of the corpus luteum. The experimental work on monkeys (as on mice) was preceded by observations on normal animals in which menstrual cycles without ovulation were demonstrated, indicating that the corpus luteum was not essential to menstrual function.

Much opposition immediately arose from clinical sources to the radical idea that the follicular hormone alone was sufficient to explain the fundamental mechanism of menstruation. Some gynecologists still call menstruation without ovulation a pseudomenstruation, although it is difficult or impossible to distinguish it externally from menstruation following ovulation. It is true, of course, that the corpus luteum hormone, progesterone, is necessary to transform the endometrium into its progestational condition (Corner and Willard Allen,[14] Hisaw and his collaborators [15]). Also progesterone will hold off or postpone the menstruation which follows withdrawal of estrogen, as shown by Smith and Engle [16] and by Hisaw.[17] But so will continued injections of estrogen. The endometrium can be kept growing for months without menstruation in castrate monkeys if the dose of estrogen is raised and maintained.[18] Also the male hormones testosterone and androsterone will postpone menstruation after withdrawal of estrogen.

Again in the experiments with estrogens in adult monkeys,[12] although menstruation was the most obvious external character, the principal point emphasized was the growth induced by the hormone in the female genital organs.[2]

*Accelerated Prepubertal Growth.*—It is also possible by injecting small amounts of estrogen to induce the prepubertal growth of the genital organs in both rodents [19] and primates.[20] This was done experimentally with estrogen before the gonadotropic function of the pituitary was discovered, with the work of Smith and Engle,[21] Zondek and Aschheim,[22] Hisaw [23] and others on the anterior pituitary gonadotropic hormone; that is, the latter segment of the endocrine chain, the ovarian-genital tract reaction, was worked out and ready for association with the anterior pituitary ovarian reactions.

*Mammary Growth.*—In the monkey the mammary glands react to estrogen alone by growth of both ducts and alveoli.[12] In some animals it apparently requires the additional action of progesterone for full growth of the alveoli, just as it does for production of a progestational endometrium.

## EARLY ATTEMPT AT CERVICAL CANCER

The beginning of my point of view on experimental cancer was an appreciation of the estrogenic hormone as a stimulator of growth of female genital tissues and the vague recognition that a definition of cancer must include the matter of growth—excessive and atypical growth. At a meeting at which the early recognition of cervical cancer was the subject, lantern slides were shown of precancerous conditions of the uterine cervix. A condition of leukoplakia was described and the development of many epithelial pegs along the base of a hypertrophied epithelium was emphasized. These sections were quite suggestive of results obtained in the cervix of the monkey by estrogenic stimulation. They raised the question "Why not try excessive estrogenic stimulation for a long period of time to see if further abnormal growths might be produced?" With Dr. Overholser a series of experiments was begun which consisted of daily injections of estrogens for several months. Some of the experiments were carried beyond a year. Abnormal growths including metaplasia of the cervical glands and marked epithelial overgrowth were induced [24] and were diagnosed histologically by others as precancerous.

*Lacassagne's Work.*—At this time (1932) Lacassagne [25] published his successful experiments which recorded the occurrence of mammary cancer in male mice which had been feminized by injections of estrogenic hormones. Estrogen stimulated growth in the mammary rudiments of the male until they were equivalent to the mammary glands of adult females, and then a considerable percentage of the males died of mammary cancer.

*Work at Yale.*—Complete confirmation of this work of Lacassagne's has been possible at Yale. In the early stages of work at Yale (1933) it became possible to

12. Allen, Edgar: The Menstrual Cycle of the Monkey Macacus Rhesus: Observations on Normal Animals, the Effects of Removal of the Ovaries and the Effects of Injections of Ovarian and Placental Extracts into the Spayed Animals, Contrib. Embryol. (No. 98), Carnegie Inst. Washington **19**: 1, 1927.

13. Werner, A. A., and Collier, W. D.: The Effect of Theelin Injections on the Castrated Woman, J. A. M. A. **100**: 633 (March 4) 1933.

14. Corner, G. W., and Allen, W. M.: Physiology of Corpus Luteum: II. Production of a Special Uterine Reaction (Progestational Proliferation) by Extracts of the Corpus Luteum, Am. J. Physiol. **88**: 326 (March) 1929.

15. Hisaw, F. L.; Meyer, R. K., and Weichert, C. K.: Inhibition of Ovulation and Associated Histological Changes, Proc. Soc. Exper. Biol. & Med. **25**: 754, 1928. Hisaw, F. L.: The Corpus Luteum Hormone: I. Experimental Relaxation of the Pelvic Ligaments of the Guinea Pig, Physiol. Zoöl. **2**: 59 (Jan.) 1929.

16. Smith, P. E., and Engle, E. T.: Prevention of Experimental Uterine Bleeding in Macacus Monkey by Corpus Luteum Extract (Progestin), Proc. Soc. Exper. Biol. & Med. **29**: 1225 (June) 1932.

17. Hisaw, F. L.: The Physiology of Menstruation in Macacus Rhesus Monkeys, Am. J. Obst. & Gynec. **29**: 638 (May) 1935.

18. Zuckerman, Solly: Inhibition and Induction of Uterine Bleeding by Means of Estrone, Lancet **2**: 9 (July 4) 1936.

19. Allen, Edgar, and Doisy, E. A.: The Induction of a Sexually Mature Condition in Immature Females by Injection of the Ovarian Follicular Hormone, Am. J. Physiol. **69**: 577 (Aug.) 1924.

20. Allen, Edgar: Reactions of Immature Monkeys (Macacus Rhesus) to Injections of Ovarian Hormone, J. Morphol. **46**: 479 (Dec. 5) 1928.

21. Smith, P. E., and Engle, E. T.: Experimental Evidence Regarding the Role of the Anterior Pituitary in the Development and Regulation of the Genital System, Am. J. Anat. **40**: 159 (Nov.) 1927.

22. Zondek, Bernhard, and Aschheim, Selmar: Ovarialhormon, Wachstum der Genitalien, sexuelle Frühreife, Klin. Wchnschr. **5**: 2199 (Nov. 19) 1926.

23. Hisaw, F. L.; Fevold, H. L., and Leonard, S. L.: Effects of Hypophysial Extracts on Sexually Immature Monkeys, Proc. Soc. Exper. Biol. & Med. **29**: 204 (Nov.) 1931.

24. Overholser, M. D., and Allen, Edgar: Atypical Growth Induced in Cervical Epithelium of Monkey by Prolonged Injections of Ovarian Hormone Combined with Chronic Trauma, Surg., Gynec. & Obst. **60**: 129 (Feb.) 1935.

25. Lacassagne, A.: Apparition de cancers de la mamelle chez la souris mâle, soumise à des injections de folliculine, Compt. rend. Acad. d. sc. **195**: 630 (Oct. 10) 1932.

affiliate Dr. L. C. Strong, a geneticist and former associate of C. C. Little, with the Department of Anatomy. Dr. Strong brought with him a colony of inbred cancer mice which seem to have many types of cancer known in human beings. We also obtained the collaboration of Dr. William U. Gardner, who had studied at the University of Missouri with Dr. Turner the responses of the mammary tissue to estrogen and other hormones. Then Dr. G. M. Smith, surgeon and pathologist, who was formerly a member of Dr. Opie's department at Washington University in prewar days and a former director of research at Barnard Hospital, collaborated as pathologist. Without his point of view as pathologist, those of us without clinical training might well have hesitated in embarking on investigations of cancer. Then Drs. William Greulich, Carroll Pfeiffer and Warren Nelson were added to our group [26] and an intensive attempt to produce cancer by excessive estrogenic stimulation was begun.[27]

*Inbred Strains of Cancer Mice.*—By inbreeding, involving brother to sister mating, more than a dozen different genetic strains of mice have been established with varying susceptibility and resistance to cancer.[28] Some of these are as different in characteristics and reactions as are Negroes and white persons. While mammary cancer has been studied most intensively, there are other types of cancer represented in these inbred mice.

In one strain of inbred mice, mammary cancer appears spontaneously in more than 80 per cent of all females before the age of 12 months. It requires only a few weeks for a small palpable nodule to become a large mammary cancer and not very much longer before the mouse dies of this cancer. The inheritance of this disease has been followed through more than forty generations, and in each generation one or more of the females have died of mammary carcinoma.

*Sexual Cycles in Cancer Mice.*—A challenging question was "What happens to the reproductive system when mammary cancer begins to grow rapidly and to produce a serious drain on the body?" It was known that estrogenic hormones stimulate growth of the mammary glands. Does rapid growth of mammary tissue in a cancer upset the endocrine balance necessary for rhythmic estrous functions in uterus and vagina, which also require estrogenic hormone? Estrous cycles were recorded in cancer mice as soon as the tumors became palpable. As the tumors grew rapidly, the estrous cycles lengthened, became irregular and in some cases disappeared altogether. Microscopic sections showed the vagina and uterus to be very atrophic, similar to the condition of castrate animals, and the ovaries to be very small, like those of very old mice. These animals were by no means old enough to have reached the natural menopause (if one may use that term for a mouse).

Injections of estrogens into these cancer mice induced full estrous growth in both vagina and uterus and secretion in the uterus.[29] Estrogenic treatment did not seem to affect the growth of the cancerous nodules. Implants of anterior pituitary tissue stimulated the ovaries to follicular growth with, secondarily, estrous conditions in the vagina and uterus. Therefore, both genital tract and gonads in these cancer mice were still reactive. The premature senility of the genital tract was apparently due to inadequate supply of ovarian and anterior pituitary hormones.

*Survey of Mammary Glands in Ten Strains of Mice Varying in Susceptibility to Cancer.*—While attempting to repeat Lacassagne's observations, a thorough search was made for differences in the mammary glands of ten strains of mice—some cancer susceptible and others cancer resistant.[30] Whole mounts of all the mammary tissue in these animals at representative stages of life were studied and foundations of normal conditions laid for later studies of mammary cancer. Many interesting things have been found such as (1) failure of development of the third pair of nipples in one particular strain of mice, (2) failure of some mammary gland rudiments of the male to respond to estrogens while others in the same mouse did respond and (3) persistence of hyperplastic nodules in involuting mammary glands of old mice which seem peculiar to animals of cancer susceptible strains. The existence of multiple hyperplastic nodules at this age provides several potential loci for cancer, and when one grows rapidly into a cancer and is removed another may accelerate growth and become lethal. This is not due to metastases but to multiple hyperplastic loci, with potentialities for development into cancer.

*Mammary Cancer in Feminized Male Mice.*—Lacassagne's report of mammary cancer in male mice feminized by injections of estrogens has been completely confirmed.[31] This has been done not only in strains of mice genetically cancer susceptible but also in strains of mice in which mammary cancer in the females is normally low (less than 5 per cent). It has not been possible to obtain mammary cancer in some of the strains which are cancer resistant, chiefly because they do not tolerate the estrogenic treatment; i. e., they die before the cancer age when on estrogen treatment which other strains tolerate. It has also been possible to define the optimum dose for mammary carcinogenesis following estrogenic treatment; i. e., there is a dosage level above that required for experimental estrous cycles which is not carcinogenic in these mice.

*Endocrine Evidence from Spontaneous Tumors.*—There is evidence from the study of gonadal tumors that endocrine imbalance may be associated with spontaneous tumors; for instance, the secretion of estrogens by testicular tumors. Of extreme interest in relation to intersexual conditions has been the finding of male dogs with mammary hypertrophy.[32] These males were treated as bitches by their canine suitors. On laparotomy they were found to have tumors in testicles retained in the abdomen. This seemed to be quite a clearcut case of secretion of estrogen by testicular tumors.

Another instance is a case of multiple tumors of endocrine glands and genital organs.[33] One female

26. Each of these investigators has added a specific technic and contributed much to the development of my point of view.

27. The experiments mentioned in this article were made possible by grants from the Anna Fuller Fund, the International Cancer Research Foundation, the Committee for Research in Problems of Sex of the National Research Council, the Jane Coffin Childs Memorial Fund, and the Phoid Research Fund of Yale University.

28. Strong, L. C.: The Establishment of the C3H Inbred Strain of Mice for the Study of Spontaneous Carcinoma of the Mammary Gland, Genetics **20**: 586, 1935.

29. Allen, Edgar; Diddle, A. W.; Strong, L. C.; Burford, T. H., and Gardner, W. U.: The Estrous Cycles of Mice During Growth of Spontaneous Mammary Tumors and the Effects of Ovarian Follicular and Anterior Pituitary Hormones, Am. J. Cancer **35**: 291 (Oct.) 1935.

30. Gardner, W. U., and Strong, L. C.: The Normal Development of the Mammary Glands of Virgin Female Mice of Ten Strains Varying in Susceptibility to Spontaneous Neoplasms, Am. J. Cancer **35**: 282 (Oct.) 1935.

31. Gardner, W. U.; Smith, G. M.; Allen, Edgar, and Strong, L. C.: Cancer of the Mammary Glands Induced in Male Mice Receiving Estrogenic Hormone, Arch. Path. **21**: 265 (March) 1936.

32. Greulich, W. W., and Burford, T. H.: Testicular Tumors Associated with Mammary, Prostatic and Other Changes in Cryptorchid Dogs, Am. J. Cancer **28**: 496 (Nov.) 1936.

33. Gardner, W. U.; Strong, L. C., and Smith, G. M.: An Observation of Primary Tumors of the Pituitary, Ovaries, and Mammary Glands in a Mouse, Am. J. Cancer **28**: 541 (March) 1936.

mouse had five cancerous nodules of the mammary gland, granulosa cell tumors in both ovaries, a pituitary gland fourteen times as large as normal and the uterus in an extremely cystic and hyperplastic condition. The endocrine relation of pituitary, ovaries, uterus and mammary glands is now well established. Cystic hyperplasia of the uterus has been induced by excessive treatment with estrogens. Pituitary hypertrophy and frank pituitary tumors have also been reported after excessive estrogenic stimulation; in our colony, however, in only one strain of mice and not in others. Granulosa cell tumors of the ovary secrete ovarian hormone, for when transplanted into male mice they induce growth of the mammary rudiments of the host. This reaction will indicate smaller amounts of estrogen than required for estrous growth of the vagina, but it requires two weeks as compared with two days for the latter.

### FURTHER EXPERIMENTS IN MONKEYS AND RABBITS

Meanwhile, further experiments were in progress with monkeys and rabbits in which estrogenic stimulation of mammary glands was studied. In young male monkeys with rudimentary glands it requires from six to eight months and a total dose of 80,000 international units of estrogen for growth equivalent to that of the adult nonpregnant female.[34] At the end of eight months of continuous estrogenic treatment of young female monkeys the mammary glands are still growing rapidly, while the uterus is small, atrophic and fibrotic—perhaps exhausted from too much estrogenic stimulation. The endometrium is so atrophic that menstruation does not follow cessation of estrogenic treatment. This is an interesting example of differential thresholds of hormone for uterus and mammary glands.

If large amounts of estrogen are injected, maintaining the hormone level considerably above normal for a long time, atypical mammary growths similar to "the witch's broom" on the willow tree may appear. One specimen was obtained from a rabbit, after injection of 5,000 international units of estrogen a week for ten months, in which three fourths of the gland was a new and quite atypical growth from a single branch of a duct of the original gland.

### STUDIES OF GROWTH WITH THE COLCHICINE TECHNIC

While attempting to produce genital cancers experimentally, studies of normal growth responses to estrogens were continued. One always welcomes a chance to restudy a question with an improved technic. This opportunity opened following description of the colchicine technic, discovered by Dustin[35] and Lits[36] at the University of Brussels and advanced by studies of Ludford[37] in England. We[38] applied this technic to a study of the reaction of the genital tissues of the mouse and monkey to estrogens. Colchicine, in the proper dose, arrests cells in mitosis, thus summarizing the dividing cells for eight or ten hours or more. This makes it possible to distinguish the part of growth in an organ (defined as increase in size) which is due to actual cell division from that which is due to other factors, such as (1) increased blood supply, (2) increased tissue fluids or (3) enlargement of cells—for all these factors are included when weights of organs are used as criteria of growth. In other words, it distinguishes hyperplasia from hypertrophy.

*Seriation of Responses to Estrogen.*—Several interesting points have been obtained by seriation of responses to estrogen. For instance, we are now able to seriate properly responses of tissues to estrogenic hormones. One of the first things that follows injection of estrogen into ovariectomized females is dilatation of the vessels which supply the genital organs. This begins within thirty minutes after subcutaneous injection. Vasodilatation is followed by an increase in the tissue fluids, especially in the connective tissues. Then, with the use of the colchicine technic, the beginning of cell division can be located accurately. In the castrate mouse, mitosis begins first in the lateral walls of the vagina and then in the tips of the glands of the uterus. After an initial period of glandular growth, cell division stops in the glands and they begin secreting, while cell division continues in the superficial endometrium. The wave of growth can also be quantitated in the vagina and in the "sexual skin" of monkeys.

*New Evidence for Difficult Questions.*—It had been suspected that a wave of growth would extend up into the uterine tubes to replace some of the cells which are eliminated in the degenerative stage of the cycle, but it had not been possible to obtain adequate evidence for such replacement. By the use of the colchicine technic it has been possible to show that at certain times these epithelial cells are replaced by cell division.[39] The limits of this wave of cell divison in the tubes have not yet been clearly defined. Controls injected with colchicine in which tubes contained few cells in mitosis lead to the conclusion that colchicine alone does not stimulate cell division in these organs. It has been clear, however, that the uterotubal junction is often a sharp dividing line between a rapidly growing uterine mucosa and a quiescent tubal epithelium. There is some sort of growth differential at this point.

*Trauma Stimulates Growth.*—With the colchicine technic it has been demonstrated that stimulation of certain tissues by trauma, as well as by hormones, will induce growth. For instance, Dr. Doisy showed that sampling vaginal contents of test rats with cotton swabs would induce enough growth in the vaginal wall to give false positives in test animals. Partial growth can easily be demonstrated and the extent of cell division shown by use of the colchicine technic.[40] Also mitosis in muscle fibers of the uterus follows both hormonal stimulation and the traumatic stimulation by distention of the uterus with paraffin pellets.[41] Apparently several stimuli that increase blood supply will induce cell division in tissues in which

34. Gardner, W. U., and Van Wagenen, G.: Experimental Development of the Mammary Gland of the Monkey, Endocrinology **22**: 164 (Feb.) 1938.

35. Dustin, A. P.: La radiothérapie et la chimiothérapie envisagées à la lumière des travaux sur les chocs caryoclasiques, J. sc. méd. de Lille, 1934, No. 49, pp. 561-573.

36. Lits, F.: Contribution à l'étude des réactions cellulaires provoquées par la colchicine, Compt. rend. Soc. de biol. **115**: 1421, 1934.

37. Ludford, R. J.: Action of Toxic Substances upon Division of Normal and Malignant Cells in Vitro and in Vivo, Arch. f. exper. Zellforsch. **18**: 411, 1936.

38. Allen, Edgar, and Creadick, R. N.: Ovogenesis During Sexual Maturity: The First Stage, Mitosis in the Germinal Epithelium, as Shown by the Colchicine Technic, Anat. Rec. **69**: 191 (Sept. 25) 1937. Allen, Edgar; Smith, G. M., and Gardner, W. U.: Accentuation of the Growth Effect of Theelin on Genital Tissues of the Ovariectomized Mouse by Arrest of Mitosis with Colchicine, Am. J. Anat. **61**: 321 (July) 1937. Worthington, R. V., and Allen, Edgar: Growth of Genital Tissues in Response to Estrone as Studied by the Colchicine Technic, Yale J. Biol. & Med. **12**: 137 (Dec.) 1939.

39. Allen, Edgar: Hyperplasia in the Epithelium of the Uterine Tubes, Am. J. Obst. & Gynec. **35**: 873 (May) 1938.

40. Rogers, P. V., and Allen, Edgar: Epithelial Growth Caused by Stimulation with Various Smear Methods as Demonstrated by Mitotic Stasis with Colchicine, Endocrinology **21**: 629 (Sept.) 1937.

41. Allen, Edgar; Smith, G. M., and Reynolds, S. R. M.: Hyperplasia of Uterine Muscle, as Studied by Colchicine Method, Proc. Soc. Exper. Biol. & Med. **37**: 257 (Oct.) 1937.

growth is normally dominated by hormones. This need not necessarily mean that the action of estrogens is merely vasodilator.

The discoverers of the colchicine technic, in attempting to explain the great numbers of mitoses in certain tissues, have suggested that the drug may stimulate mitosis in cells which already have "a blastic potentiality." On the contrary, genital tissues of control castrate mice and monkeys injected with colchicine alone show very little cell division. Apparently they haven't the "blastic potentialities" until stimulated by the hormone or by other stimuli. The controls for these experiments give clearly negative results. When one appreciates that the vagina of a mouse stimulated by estrogenic hormone will grow from two to more than twelve layers of cells in forty-eight hours, there is no need to consider colchicine as used in our experiments a stimulator of mitosis.

### SKELETAL ALTERATIONS INDUCED BY ESTROGENS

Estrogens have marked effects on tissues not primarily reproductive. Modification of the pelvis by hormone action to enlarge the birth canal in certain animals is well known. Examples are (1) the resorption of the symphysis pubis of the female pocket gopher at the time of puberty [42] and (2) the relaxation of the pelvic ligaments of the guinea pig.[43] Both can be produced experimentally by injecting hormones.

Mice, males as well as females, on intensive and extended treatment with estrogens undergo complete resorption of the osseous symphysis pubis.[44] The only bond across the ventral midline is ligamentous. The resorption is so extensive that some of the ventral muscles that were previously attached to the pelvis then take their attachment from the ligamentous bond.

*Formation of New Bone in the Marrow Cavities.*—While the bone of the symphysis pubis is being resorbed during estrogenic treatment, new bone is being laid down in the marrow cavities of other bones.[45] In extreme experimental cases the marrow cavities have been completely replaced by formation of new bone. Then, searching in normal mice, it was found that spicules of new bone formed in untreated females toward the end of pregnancy. In normal pigeons and sparrows at the time of egg laying the marrow cavities also show evidence of new bone formation. Serum calcium and phosphorus levels did not rise appreciably in the blood of experimental mammals during this new formation, but in birds on estrogenic treatment these levels can be doubled or even tripled. The lipoids in the serum may also reach a high concentration.

When male sex hormone is injected simultaneously with effective doses of estrogen the skeletal changes are prevented, both the resorption of the symphysis pubis and the formation of new osseous tissue in the marrow cavities of other bones.[46] This explains why it requires higher estrogenic levels to induce these changes in the skeletons of males than in females.

*Osteogenic Sarcomas.*—Pybus and Miller (1938) observed a strain of mice in which 80 per cent of the females died with osteogenic sarcomas and in which less than 20 per cent of the males were similarly affected. The injection of estrogens in males of this strain increased the tumor incidence up to that of the females.[47] As yet, osteogenic sarcomas have not appeared in our colony of mice.

### TESTICULAR TUMORS

Long-continued injections of estrogens into the A strain of mice have a very definite effect on the testes. This treatment is followed first by hypertrophy of interstitial tissues and damage to spermatogenic tubules. In some cases the tubules are entirely destroyed and the testes become nothing but hyperplastic masses of interstitial tissue.[48] They might truly be called testicular tumors.

### FIBROMYOMAS OF THE UTERUS

Long-continued injections of estrogens in guinea pigs have been followed by development of multiple fibromyomas of the uterus.[49] After injection of as much as 50 rat units daily for eight months, the first sign of abnormality was the appearance of extensive bleeding from the vagina, just as in cases of uterine fibroids in women. Laparotomy showed multiple button-like fibromyomatous tumors on the peritoneal surfaces of the uterine cornua. These tumors did not extend into the lumen of the uterus. Whether bleeding from the endometrium is causally related to the tumor masses or merely a parallel development is uncertain.

In the guinea pig there is an extreme epithelial growth of the cervix with metaplasia, pearl formation and other conditions similar to those found in the monkey, but even more extreme. I know of no cases yet of cervical carcinoma in guinea pigs. It is of interest to note that extended treatment with estrogen at high levels has so far failed to produce uterine fibromyomas in mice, rats and monkeys. Why should the guinea pig seem especially susceptible to uterine fibromyomas, as apparently are Negro women?

### CERVICAL CARCINOMA

Although attempts to produce cervical carcinomas in monkeys and guinea pigs have not yet been successful in demonstrating independent growths, the final proof has been obtained in mice.[50] More than twenty tumors diagnosed histologically as cervical carcinomas have appeared following long-continued estrogenic treatment. It has been possible to transplant bits of cervical carcinoma into other mice, males as well as females, and demonstrate independent growth of the cancer in the host without continued hormonal stimulation. As yet there are no cases on record of spontaneous cervical cancers in mice. It is interesting to note that mammary cancer developed in some of these animals and had to be removed surgically to allow the animal long enough life for growth of the cervical carcinoma. There is apparently a time differential between uterine cervix

42. Hisaw, F. L.: The Influence of the Ovary on the Resorption of the Pubic Bones of the Pocket Gopher, Geomys Bursarius, J. Exper. Zoöl. **42**: 411, 1925.

43. Hisaw, F. L.: Experimental Relaxation of the Pubic Ligament of the Guinea Pig, Proc. Soc. Exper. Biol. & Med. **23**: 661, 1926; Experimental Relaxation of the Symphysis Pubis of the Guinea Pig, Anat. Rec. **37**: 126, 1927.

44. Gardner, W. U.: Sexual Dimorphism of the Pelvis of the Mouse: The Effect of Estrogenic Hormones upon the Pelvis and upon the Development of Scrotal Hernias, Am. J. Anat. **59**: 459 (Sept.) 1936.

45. Gardner, W. U., and Pfeiffer, C. A.: Skeletal Changes in Mice Receiving Estrogens, Proc. Soc. Exper. Biol. & Med. **37**: 678 (Jan.) 1938.

46. Gardner, W. U., and Pfeiffer, C. A.: Inhibition of Estrogenic Effects on the Skeleton by Testosterone Injections, Proc. Soc. Exper. Biol. & Med. **38**: 599 (May) 1938.

47. Pybus, F. C., and Miller, E. W.: Bone Tumors and Estrone, Nature, London **142**: 872 (Nov. 12) 1938.

48. Gardner, W. U.: Hypertrophy of Interstitial Cells in the Testes of Mice Receiving Estrogenic Hormones, Anat. Rec. **68**: 339 (June 25) 1937.

49. Nelson, W. O.: Endometrial and Myometrial Changes, Including Fibromyomatous Nodules, Induced in the Uterus of the Guinea Pig by the Prolonged Administration of Estrogenic Hormone, Anat. Rec. **68**: 99 (April 25) 1937.

50. Gardner, W. U.; Allen, Edgar; Smith, G. M., and Strong, L. C.: Carcinoma of the Cervix of Mice Receiving Estrogens, J. A. M. A. **110**: 1182 (April 9) 1938. Gardner, W. U., and Allen, Edgar: Malignant and Nonmalignant Uterine and Vaginal Lesions in Mice Receiving Estrogens and Estrogens and Androgens Simultaneously, Yale J. Biol. & Med. **11**: 213 (Dec.) 1939.

and mammary glands. Also genetic susceptibility or resistance to spontaneous mammary cancer does not seem to be related to cervical carcinoma experimentally produced by estrogens.

Recently Dr. Gardner has completed a series of injections in which male hormone was injected simultaneously with estrogen. The incidence of cervical carcinoma in these mice was higher than in the series in which estrogen alone was used. Perhaps this increased incidence was due to the fact that mammary cancer does not develop in the estrogen-androgen animals and consequently these animals live longer than the estrogen series.

### MAMMARY CANCER FOLLOWING METHYLCHOLANTHRENE

In some strains of mice in which mammary cancer seldom appears spontaneously, and which are resistant to mammary cancer after treatment with estrogens, mammary cancer may be induced by injecting the carcinogen methylcholanthrene.[51] That the reaction may be systemic as well as local is shown by the appearance of mammary cancer following application of the carcinogen to the skin of the back.

### ARE ESTROGENS CARCINOGENIC?

Many different estrogenic chemicals have been tried as to their ability to produce cancer. So far at least a dozen, including the recently discovered synthetic estrogen stilbestrol, although they have different potencies, have induced these abnormal growths.[52]

### ATYPICAL CONDITIONS PRODUCED BY ENDOGENOUS HORMONES FOLLOWING EXPERIMENTALLY PRODUCED ENDOCRINE IMBALANCE

A criticism of experiments with massive doses of estrogens has been that such enormous amounts as those injected could not possibly result from the secretion of endogenous hormone from the animal's own glands. Recently this objection has been met by ingenious work involving experimental production of endocrine imbalance.[53] Dr. Pfeiffer showed that in rodents there is a sexual difference in secretion of gonadotropic hormone by the pituitary. The pituitary of the male is several times more potent than that of the female. He then showed that the testis might successfully be transplanted into female mice the day after birth. These transplants, unlike the goat glands of infamous repute, become vascularized and grow normally in mice of the same inbred strain. Secretion of the transplanted testis masculinizes the female pituitary in that it induces it to secrete gonadotropic hormone at the male level. This apparently induces a hyperovarian endocrine condition and the uterus and mammary glands show atypical growths similar to those described following long-continued estrogenic injections. Therefore it is possible for endogenous hormones to produce similar changes. The inference should not be drawn that in these experiments the ovaries produced amounts of hormone equivalent to those injected in the cancer experiments. Perhaps the steady (uninterrupted) secretion by the modified glands is the important factor. Besides, no one can tell how much of the injected hormone is destroyed by the body's defense mechanism.

### GENERAL CONSIDERATIONS

I realize that "It's a long way from cancer in mice to cancer in women." I also realize that results obtained experimentally in mice may require years for confirmation in women. But surely these experiments on mice have some application clinically! And monkeys are so similar to women in reproductive function that work with them is surely at least subclinical.

The highest incidence of female genital cancer in aging persons at or after the menopause is well recognized. It is known also that ovulation usually stops after the menopause. This eliminates the possible participation of the corpus luteum hormone in periodically modifying or interrupting estrogenic stimulation. Ovarian conditions, however, especially if some cystic follicles develop, would lead one to expect a more or less continuous level of estrogenic stimulation. Therefore a hormone imbalance at this time might well be an important factor in etiology of cancer of the genital organs in women.

One of the most important problems in the matter of aging is whether or not hormone therapy should attempt to extend the function of reproductive organs by administering ovarian hormones after the menopause; that is, in the absence of clearly established pathologic changes. Use of estrogens for severe climacteric symptoms, in senile atrophy and in other conditions is well known. Moderate use of threshold doses, if not continued too long, seems entirely logical in these cases. But after the demonstration that estrogenic treatment, long continued at high levels, is followed by abnormal growths of the female genital organs, including fibroid tumors of the uterus, cervical carcinoma and mammary cancer, the following question may be asked: Is the clinician justified in prescribing enormous doses of concentrated estrogenic preparations for aging women?

Of course, there are the factors of susceptibility and resistance. Attempts to produce genital cancer with estrogens in some species of animals are still unsuccessful. A species or strain resistance seems to protect them.

The body's resistance to high doses of estrogens seems to be centered for the most part in the liver. Its function in detoxification is well established. Greene has shown in rabbits that experimental damage to the liver, similar to that which occurs in toxemias of pregnancy, decreases the effective dose of estrogen and shortens the time of appearance of mammary cancer and that an experimentally induced mastitis may produce similar results.

Again it may be pointed out that in some cases aging women have already been given massive doses of estrogen without subsequent appearance of genital cancer. The answer to this lies in an understanding of cancer incidence. When groups of mice are injected with optimum doses of estrogen for induction of mammary cancer, only a certain percentage will die of cancer. Something of genetic susceptibility or resistance to cancer in mice is known, for half a dozen generations can be bred in a year, but very little is known as yet of genetic susceptibility to cancer in human beings.

Then there is the matter of time lag or interval between a stimulus and the development of cancer, and

51. Strong, L. C., and Smith, G. M.: The Local Induction of Carcinoma of the Mammary Gland by Methylcholanthrene, Yale J. Biol. & Med. **11**:589 (July) 1939.

52. Lacassagne, A.: Apparition d'adénocarcinomes mammaires chez des souris males traitées par une substance estrogène synthétique, Compt. rend. Soc. de biol. **129**:641, 1938. Robson, J. M., and Bonser, G. M.: Production of Mammary Carcinomas in Mice of a Susceptible Strain by the Synthetic Estrogen, Triphenyl Ethylene, Nature, London **142**:836 (Nov.) 1938. Gardner, W. U.: Estrogens in Carcinogenesis, Arch. Path. **27**:138 (Jan.) 1939.

53. Pfeiffer, C. A.: The Effects of an Experimentally Induced Endocrine Imbalance in Female Mice, Anat. Rec. **75**:465 (Dec. 25) 1939.

there is much evidence to show that in man this may be a matter of years, just as with x-ray burns and radium poisoning.

I do not wish to attach an undue significance to these experimental results with estrogens. It seems to me, however, that they do indicate the possible danger of long-continued high levels of a hormone which is a natural constituent of the normal female body. These results also indicate that, unless an individual is especially susceptible, there are levels of estrogenic treatment which, so far as is known at present, are below the carcinogenic level. If therapeutic levels can be established within a safe range, the danger can be minimized.

333 Cedar Street.

## Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS.

HOWARD A. CARTER, Secretary.

### FISCHER MODEL S SHORT WAVE UNIT ACCEPTABLE

Manufacturer: H. G. Fischer and Company, 2323 Wabansia Avenue, Chicago.

The Fischer Model S Short Wave Unit is designed for medical and minor surgical diathermy. It combines the cabinet and portable features, since the section containing the short wave mechanism can be removed from the cabinet and carried. Accessories that have been tested include cuff and inductance cable electrodes. Electrosurgical accessories are also available but were not tested. The shipping weight is 122 pounds and the net weight 92 pounds.

Fischer Model S Short Wave Unit.

The apparatus is provided according to order with a 6 or 12 meter wavelength and employs two Westinghouse No. 471 oscillator tubes and two rectifier tubes in a tuned plate, tuned grid circuit. A choke coil is used in the primary circuit to reduce radio interference. The unit is ventilated by air convection. It operates on 105-120 volts, 60 cycle alternating current.

The firm submitted evidence for the claim that with an electromotive force of 115 volts and a full input load of 755 watts the output is 350 watts. The Council confirmed this power output by the conventional lamp load method, using four 100 watt tungsten filament bulbs in parallel. The final temperature of the outside windings of the transformer came within the limits of safety after the unit had been operated at full load for two hours.

The Model S has a similar circuit to the Council-accepted Model PC (THE JOURNAL, Dec. 24, 1938, p. 2393) and therefore the same evidence for the power of the unit to produce heat deep within human tissue was used for the Model S. The data are given in the accompanying tables.

*The Fischer 6 Meter Short Wave Unit, Model S*

Average temperature (F.) of six observations:

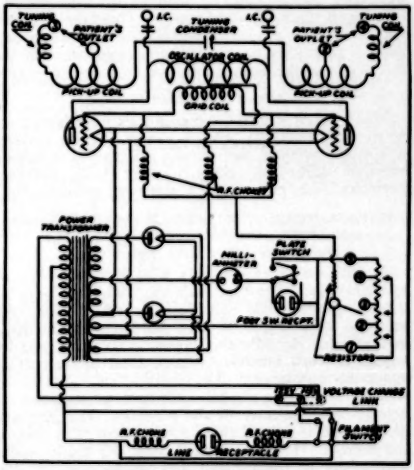
| | Deep Muscle | | Oral | |
|---|---|---|---|---|
| | Initial | Final | Initial | Final |
| Cuff technic | 99.5 | 106.8 | 98.3 | 98.8 |
| | Deep Muscle | | Oral | |
| | Initial | Final | Initial | Final |
| Inductance coil technic | 99.4 | 107.7 | 98.3 | 98.8 |

The apparatus was reported to give satisfactory clinical service in investigations conducted for the Council.

*The Fischer 12 Meter Short Wave Unit, Model S*

Average temperature (F.) of six observations:

| | Deep Muscle | | Oral | |
|---|---|---|---|---|
| | Initial | Final | Initial | Final |
| Cuff technic | 99.5 | 108.0 | 98.4 | 98.9 |
| | Deep Muscle | | Oral | |
| | Initial | Final | Initial | Final |
| Inductance coil technic | 99.5 | 107.5 | 98.7 | 99.0 |
| | Deep Muscle | | Oral | |
| | Initial | Final | Initial | Final |
| Electromagnetic field | 97.3 | 106.4 | 98.7 | 98.9 |
| | Deep Muscle | | Oral | |
| | Initial | Final | Initial | Final |
| Air spaced electrode | 97.9 | 106.1 | 98.3 | 98.5 |




Schematic diagram of circuit.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Fischer Model S Short Wave Unit, as used with the cuff and coil electrodes, for inclusion in the Council's list of acceptable devices.

### EREX HYPO-ALLERGENIC COVERS (Pillow, Mattress, Crib Covers) ACCEPTABLE

Manufacturer: Erex Hypo-Allergenic Products Company, 763 Boatman's Bank Building, St. Louis.

The Erex Hypo-Allergenic Pillow, Mattress and Crib Covers are intended to protect individuals allergic to dust from pillows and also to provide general sanitation of the pillow and its protection from perspiration. The covers are made of a rubberless fabric called "Revolite." The pillow covers are 21 by 28 inches in size and are intended to be covered by regulation type pillow cases. The mattress covers are available in twin or full bed size.

Two samples of covers were submitted to the Council, in which binding tape was used along the seams. In one, a coated tape similar to the Erex fabric was used, and in the other the customary "stay" tape. The stitching is of the lock-stitch type,

claimed to be a tighter stitch than the chain type. The pillows are closed by an invisible slide fastener and there is a "cup flap" to protect the slide fastener opening and help keep the enclosed pillow in proper place.

The firm claims that the cover is dust proof, perspiration proof and sanitary. It is advocated for asthma, hay fever and sinus sufferers. According to the producers, the covers launder well and will remain permanently soft and pliable. Evidence was submitted by the firm to show the resistance of the covers to heat and cold and a variety of chemical agents.

The covers were investigated by the Council and found to be as satisfactory as such covers probably can be made. The material composing the covers is impervious and stands washing as described in the printed matter submitted with it. When they are filled with water there is practically no leakage along the seams within several minutes. There is, however, the unavoidable leakage around the slide fastener opening. This leakage of water cannot be prevented by any flap, but the manufacturer's idea of using the cuplike flap to extend around the end of the pillow under the slide fastener makes an effective seal against dust.

The Council on Physical Therapy voted to include the Hypo-Allergenic Covers on its list of accepted devices.

## Council on Pharmacy and Chemistry

### COUNCILS' COMMITTEE ON CONTRACEPTIVES

THE FOLLOWING REPORT WAS PREPARED UNDER THE AUSPICES OF THE COUNCILS' COMMITTEE ON CONTRACEPTIVES AND PUBLICATION HAS BEEN AUTHORIZED.

PAUL NICHOLAS LEECH, Secretary
COUNCIL ON PHARMACY AND CHEMISTRY.

HOWARD A. CARTER, Secretary
COUNCIL ON PHYSICAL THERAPY.

### RUBBER SHEATHS

The condom is perhaps the simplest, most widely used contraceptive measure. When properly tested sheaths are used skilfully, the patient obtains practically complete protection. Authorities also agree, in general, that the condom is the most useful of all methods for venereal disease prophylaxis. The review by Cautley, Beebe and Dickinson[1] on the quality and effectiveness of rubber sheaths in prophylaxis was undertaken because of the widespread use of this article.

The chief difficulty of the method lies in the existence of inferior articles. Methods of manufacturing have improved considerably in the past few years when the dipping in crape rubber solution was replaced by the liquid latex method. Nevertheless a large portion of the output by the manufacturers was unreliable, as shown by careful testing. Tests conducted by Voge[2] of more than 2,000 condoms of various brands demonstrated that a large percentage of condoms were imperfect according to the Voge technic of testing, 50 per cent containing flaws.

The Food and Drug Administration has informed manufacturers that:

> Regardless of the nature of the products or methods by which they are used, all articles intended as venereal disease preventives are subject to the provisions of the act [Federal Food and Drug Act].
>
> It is the consensus of present-day medical opinion that no article which depends on its chemical action for its preventive properties is sufficiently effective against all venereal diseases to justify an unqualified claim for the prevention of venereal disease. Other articles depending for their prophylactic effect on preventing contact with infecting organisms should be free from defects.
>
> Preventive claims should be unambiguous and limited to the disease or diseases against which the article is known to be effective. The directions should be such as to insure suitable use.

In the year ended June 30, 1939, the sampling and examination of prophylactics by the Department of Agriculture resulted in the seizure of seventy-five consignments. This department is continuing to collect and examine a great many more samples. This action has resulted in some firms closing down their plants to install new machinery and improve their manufacturing processes. The more recent investigations have shown that imperfect samples are still encountered, but that the market contains a far higher quality rubber sheath than at any other time.

It is therefore anticipated that in the future most condoms purchased on the market will conform to the desired degree of quality which would make for a fairly reliable method for venereal prophylaxis as well as for purposes of therapeutic contraception.

1. Cautley, Randolph; Beebe, Gilbert W., and Dickinson, Robert L.: Rubber Sheaths as Venereal Disease Prophylactics, Am. J. M. Sc. **195**: 155 (Feb.) 1938.
2. Voge, C. I. B., quoted by Cautley, Beebe and Dickinson.[1]

## Council on Foods

### ACCEPTED FOODS

THE FOLLOWING ADDITIONAL FOODS HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO ACCEPTED FOODS.

FRANKLIN C. BING, Secretary.

#### FOODS FOR SPECIAL DIETETIC PURPOSES (*See* Accepted Foods, 1939, p. 295).

**Northwest Powdered Fruit Laboratories, Inc., Yakima, Wash.**

PO-AP, a granular form of powdered dried apple pulp from several varieties of apples. This product is useful in the dietary management of diarrhea.

*Analysis* (submitted by manufacturer).—Moisture 4.5%, total solids 95.5%, ash 1.6%, fat (ether extract) 3.4%, protein (N × 6.25) 1.5%, crude fiber 4.2%, reducing sugars before inversion 53.0%, sucrose [(total reducing sugars after inversion minus reducing sugars before inversion) × 0.95] 18.1%, pectic acid (alcohol precipitate) 3.9%, total carbohydrates other than crude fiber (by difference) 84.8%, iron (Fe) 0.00275%, calcium (Ca) 0.0204%, magnesium (Mg) 0.0282%, phosphorus (P) 0.0029%, sulfur (S) 0.032%, sodium (Na) 0.107%, potassium (K) 0.847%, chlorides (Cl) 0.21%, copper (Cu) 0.00077%, lead (Pb) none, arsenic ($As_2O_3$) 0.00015 grain per pound of apple powder, sulfur dioxide ($SO_2$) 0.005%.

*Calories.*—3.5 per gram; 99 per ounce.

#### MILK AND MILK PRODUCTS (*See* Accepted Foods, 1939, p. 230).

**Helm Goat Milk Products, Grass Lake, Mich.**

HELM'S BRAND DEHYDRATED GOAT'S MILK, a spray-dried, homogenized whole goat's milk.

*Analysis* (submitted by manufacturer).—Moisture 1.0%, total solids 99.0%, ash 6.5%, fat (ether extract) 29.0%, protein (N × 6.38) 25.0%, lactose (by difference) 38.5%.

*Calories.*—5.2 per gram; 148 per ounce.

#### VEGETABLES (*See* Accepted Foods, 1939, page 345).

**General Foods Corporation, New York,** product distributed by Frosted Foods Sales Corporation, New York.

BIRDS EYE BRAND QUICK-FROZEN GREEN PEAS, quick-frozen, ready-to-cook, green peas, conforming to the U. S. D. A. tentative standards for frozen peas, as U. S. Grade A (fancy).

*Manufacture.*—The peas are packed in a number of plants located in different sections of the United States. Trained field representatives exercise control over the selection, cultivation and harvesting of the crops, as well as the packing and freezing operations in all plants. The method of processing has been described briefly in the report of the Council on Foods [Rose, Mary S.: The Effect of Quick Freezing on the Nutritive Values of Foods, J. A. M. A. **114**: 1357 (April 6) 1940] as the indirect contact, multiple plate method, with multiple plate freezers. The blanched peas are packed in cellophane-lined cartons which are sealed in wax paper. Cartons of the finished product are transported in specially designed refrigerator cars in which the temperature is reduced to from 15.6 to 11.1 C. When the foods reach their destination they are stored at —17.8 C. until they are delivered to a distributor. Refrigerator cases are used in retail stores and in institutions to maintain the products at low temperatures. The Frosted Foods Sales Corporation provides dealers and institutions with detailed instructions for the care of the cases.

*Analysis* (submitted by manufacturer).—Average: Moisture 81.2%, total solids 18.8%, ash 0.6%, fat (ether extract) 0.5%, protein (N × 6.25) 5.2%, crude fiber 2.1%, sucrose 4.8%, reducing sugars 0.00, starch 2.3%, carbohydrates other than crude fiber (by difference) 10.4%. Range: Moisture 80.0 to 82.8%, total solids 17.2 to 19.8%, alcohol insoluble solids 12.5 to 18.0%, ash 0.5 to 0.6%, fat (ether extract) 0.4 to 0.6%, protein (N × 6.25) 4.9 to 5.5%, crude fiber 1.8 to 2.3%, sucrose 4.4 to 5.4%, reducing sugars 0.00, starch 1.8 to 3.2%, carbohydrates other than crude fiber (by difference) 9.6 to 10.8%.

The firm reports (1939) the vitamin content to be as follows (fresh basis): vitamin A from 3.0 to 5.5 micrograms of beta carotene (equivalent to from 5 to 9.1 international units) per gram, vitamin $B_1$ from 1.0 to 1.5 international units per gram, vitamin G (riboflavin) from 0.7 to 1.0 Sherman-Bourquin units per gram, vitamin C from 0.13 to 0.26 mg. of ascorbic acid (equivalent to from 0.65 to 1.30 international units) per gram.

*Calories.*—Average: 0.67 per gram; 19.03 per ounce. Range: 0.62 to 0.68 per gram; 17.6 to 19.3 per ounce.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 NORTH DEARBORN STREET - - - CHICAGO, ILL.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Eight dollars per annum in advance

*Please send in promptly notice of change of address, giving both old and new; always state whether the change is temporary or permanent. Such notice should mention all journals received from this office. Important information regarding contributions will be found on second advertising page following reading matter.*

SATURDAY, MAY 25, 1940

## THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

**The American Medical Association advocates:**

**1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.**

**2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.**

**3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.**

**4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.**

**5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.**

**6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.**

**7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.**

**8. Expansion of public health and medical services consistent with the American system of democracy.**

## THE PHARMACOPEIAL CONVENTION OF 1940

Last week approximately 500 representatives of medicine, pharmacy and related sciences assembled in Washington to constitute the decennial U. S. Pharmacopeial Convention. Ten years has elapsed since the last previous convention, which THE JOURNAL described as a farcical assemblage if considered from the point of view of scientific progress. Industrial interests overwhelmed that convention with representatives; the ratio of pharmaceutic interests to scientific medicine was about five to one. The results were fortunately not as disastrous as then seemed likely because a number of faithful and competent workers, appointed to the Revision Committee, sacrificed time and effort to bring forth a creditable pharmacopeia.

The Pharmacopeia is vital to physicians because it establishes the legal standards under which the United States government enforces the purity of official drugs in interstate commerce. Because of its particular significance to the practice of medicine, the American Medical Association through its Board of Trustees, its Council on Pharmacy and Chemistry and THE JOURNAL, has always urged efforts toward the development of the best pharmacopeia possible for the needs of modern medicine. This year, by editorials in THE JOURNAL and by correspondence, every reputable medical school and every state medical association was urged to send delegates. The delegation was much larger than ten years before but still not as large as it should have been. The spirit of the convention was far different from that which prevailed previously. The report of the president of the convention, Dr. Walter A. Bastedo, was followed by papers by Dr. Morris Fishbein of the American Medical Association delegation, by Mr. E. F. Kelly, representing the American Pharmaceutical Association delegation, and by Mr. W. G. Campbell, commissioner of the Food and Drug Administration. Two of these papers emphasized the unwieldy character of the convention and the need for modernizing its methods of procedure. These suggestions were received cordially by the reference committee to which the papers were referred and endorsed by the convention. The delegation of the American Medical Association presented, and the convention adopted, the following resolution:

*Resolved*, That the President and the Board of Trustees be authorized to appoint a committee of nine, consisting of four physicians, four pharmacists and one representative of a governmental agency, and including the president, the secretary and the chairman of the revision committee, ex officio, to make a revision of the constitution and by-laws of the United States Pharmacopeial Convention; and

That this revision be submitted to the convention at a special session to be called by the Board of Trustees not more than two years from the date of adjournment of this session; and

That the following principles be considered in the preparation of this proposed revision:

1. The development of a representative body of a size capable of functioning efficiently.

2. Suitable and proportional representation for medicine, pharmacy, dentistry, veterinary medicine, governmental agencies and manufacturing pharmacy.

3. Selection of well qualified experts to undertake the necessary periodic revisions of the Pharmacopeia.

4. Selection of a governing body or board of trustees with continuous overlapping terms of office to provide for continuity of policy and action.

5. Revision and publication every five years with interim supplements.

6. Establishment of fundamental criteria for admission of drugs and preparations to the Pharmacopeia.

7. Establishment of a full time executive staff without personal affiliation with any private agency.

Mr. Campbell emphasized the fact that establishment of standards for drugs was wholly within the purview of the convention and that the Food and Drug Administration had no disposition to dominate in any way the

action of the Revision Committee of the Pharmacopeia unless there should arise some emergency in which public health would demand action. Even in this event, he said, any action would be taken only after consultation with the Pharmacopeial authorities.

The convention also changed a number of the by-laws of procedure; the changes will presumably be in effect until a new constitution and by-laws are adopted. Hereafter each delegation will be entitled to only one vote. This was in conformity with the suggestions which had been made repeatedly by THE JOURNAL.[1] It was tacitly understood that the Committee on Revision would be composed of one-third medical representatives and two-thirds pharmacists, but that the medical representatives would have full control on questions of therapeutic scope.

Dr. C. W. Edmunds, who has served long and well as a member of the Revision Committee, was chosen president of the convention for the next decennial period. The Board of Trustees (composed of two physicians and three pharmacists) now consists of Dr. Walter A. Bastedo, Dr. Morris Fishbein, editor of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Mr. Robert L. Swain, editor of *Drug Topics* and *Drug Trade News*, Mr. E. F. Kelly, secretary of the American Pharmaceutical Association, chairman, and Dr. E. E. Little, dean of the Rutgers School of Pharmacy. The members of the Revision Committee, whose names appear elsewhere in the news columns of THE JOURNAL, chose Dr. E. Fullerton Cook to continue in the important position of chairman of the Revision Committee. Dr. Cook has ably conducted the revision of the Pharmacopeia in the last decade and a half.

The 1940 convention may well stand in medical and pharmaceutic history as a turning point toward progressive procedure in the formulation of this important compendium. If a new constitution and by-laws are adopted in accordance with the instructions of the convention, work will be facilitated, self seeking will be discouraged and a scientific spirit will be maintained. No longer will there be the difficult task of securing sufficient representation in medicine and progressive pharmacy for a meeting in which predatory interests might otherwise overrule the decisions. Proportionate representation will undoubtedly be provided on a scale which will develop a smaller and more efficient assemblage. In the future, no doubt, members may be chosen for the Revision Committee on the basis of competence primarily rather than because of ability to attend the convention. The best men available should aid in the revision. The Pharmacopeial Convention of 1940 represents the fruitful union of the most progressive elements of both medicine and pharmacy and should result in the production of the best pharmacopeia in the world.

1. The Call for the Pharmacopeial Convention of 1940, editorial, J. A. M. A. **112**:1969 (May 13) 1939. Physician and Pharmacopeia, ibid. **113**:2323 (Dec. 23) 1939.

## CHEMOTHERAPY OF INFECTIOUS DISEASES

In 1904 Ehrlich summarized the aims of chemotherapy: "What we seek is 'specific chemotherapy,' that is, we are in the search of a drug which should be capable of destroying certain parasites without at the same time causing too much damage to the host." Since that time chemotherapy has accomplished notable successes in the treatment of diseases caused by protozoa and spirochetes and more recently by other bacteria. The use of organic arsenical compounds in the treatment of syphilis, of plasmochin and atabrine in malaria, of quinoline derivatives in ameba amebiasis and of antimony compounds in the treatment of leishmaniasis is well established. In the case of bacterial disease the problem proved to be much more difficult because the organisms are much less differentiated. Koch's failure to cure guinea pigs infected with anthrax by injection of mercuric salts discouraged, at least temporarily, much research in this field.

The preparation by Gelmo in 1908 of the compound para-aminobenzenesulfonamide in the course of a purely scientific research not at all concerned with problems of chemotherapy resulted, nevertheless, in a renewed interest in the search for new chemotherapeutic agents. Hörlein, Dressel and Kothe of the I. G. Farbenindustrie prepared new textile dyes from azo compounds containing sulfonamide groups. Eisenberg demonstrated the bactericidal action of certain azo compounds in vitro and employed chrysoidin for chemotherapeutic purposes. American investigators, Heidelberger and Jacobs, linked dihydrocupreine with diazo compounds obtained from aromatic amines, including para-aminobenzenesulfonamide, and found that many of the azo compounds thus formed exhibited bactericidal properties in vitro but not in vivo. A number of azo compounds were found in the laboratories of I. G. Farbenindustrie to possess bactericidal properties in vitro. Compounds containing the sulfonamide group were found to be effective against streptococcic infection in animal experiments. The chemists Klarer and Mietzsch synthesized sulfonamide containing azo compounds, and Domagk demonstrated that one of these products was effective in preventing death in mice infected with lethal doses of streptococci. Their collaboration led to the development of a product patented as "Prontosil" and somewhat later to "Prontosil Soluble." At about the same time Trefouel and his associates in France established that a number of azo dyes prepared from para-aminobenzenesulfonamide but of different physical and chemical properties had an antistreptococcic action like that of "Prontosil." They have advanced the hypothesis that all the active azo dyes, including "Prontosil," were reduced in the organism to sulfanilamide. This led them to the important discovery that the simple

colorless compound sulfanilamide was itself highly active as a therapeutic agent in experimental streptococcic infection. Domagk's contribution, as Heubner points out, consists in establishing the fact that of the many tested substances the derivatives of sulfanilamide alone possess the property of favorably influencing streptococcic infection in the mouse, the rabbit and man.

The dramatic results obtained with sulfanilamide in many instances in a variety of streptococcic infections such as puerperal fever, meningitis, septicemia, erysipelas, scarlet fever and osteomyelitis and in gonorrhea are now common knowledge attested by an overwhelming literature. The new derivative sulfapyridine has been found to be strikingly effective in pneumococcic pneumonia. The most recent derivative, sulfathiazole, appears to be as effective against pneumococcic infection as sulfapyridine but is superior to both sulfapyridine and sulfanilamide against staphylococcic infection.

Empiricism, however, has definite limitations. It is realized that further knowledge can come only from understanding the mode of action of these compounds. This subject was editorially discussed in THE JOURNAL,[1] but for a more detailed exposition one should consult the reviews by Domagk,[2] by Marshall,[3] and a recent one by Heubner.[4] A genuine bactericidal effect of sulfanilamide on the cocci has not been demonstrated. The effect is rather that of arrest of growth, due possibly to disturbance of metabolism or to interference with the capsule formation of the cocci. R. L. Mayer [5] pointed out that the frequent appearance of methemoglobin in the blood of animals and patients treated with sulfanilamide suggests the formation in the body of a product of the drug responsible for the formation of methemoglobin. He advanced the hypothesis that the bactericidal effect is due not to sulfanilamide but to the same oxidative product which oxidizes hemoglobin to methemoglobin. This theory is further developed by Shaffer,[6] who states that the probable mode of action of sulfanilamide is that the drug provides a mechanism by which the sterilizing oxidation intensity of molecular antigen is applied merely at its maximum to bacteria and unfortunately also, to some extent, to host cells. The present status of our knowledge is summed up by Marshall in his review of the pharmacology of sulfanilamide: "No satisfactory explanation of the mechanism of action has been found." There is, however, little doubt that the advent of sulfanilamide has initiated a true renaissance of bacterial chemotherapy.

1. Mode of Action of Sulfanilamide, editorial, J. A. M. A. **111**: 2304 (Dec 17) 1938.
2. Domagk, G.: Chemotherapie der bakteriellen Infektionen, Angewandte Chemie **52**: 657 (Oct. 19) 1935.
3. Marshall, E. K., Jr.: Bacterial Chemotherapy: The Pharmacology of Sulfanilamide, Physiol. Rev. **19**: 240 (April) 1939.
4. Heubner, W.: Chemotherapie von Infektionskrankheiten, Klin. Wchnschr. **19**: 265 (March 23), 289 (March 30) 1940.
5. Mayer, R. L.: Recherches sur le mecanisme de l'action antistreptococciques, Biol. méd. **27** (supplement): 45, 1937.
6. Shaffer, P. A.: The Mode of Action of Sulfanilamide, Science **89**: 547 (June 16) 1939.

## HEPARIN

As a result of the rapidly developing information concerning this substance during recent years, heparin, from being a rather unique anticoagulant with limited laboratory application, has become a promising clinical adjunct. The isolation of a highly purified product has contributed to the advance in our knowledge of this substance. The rapidly accumulating information regarding heparin has recently been reviewed by the Scandinavian investigator Jorpes.[1]

With the purified product available, organic chemists have made progress in establishing the chemical structure of the heparin molecule. Thus Charles and Todd [2] have studied the crystalline barium salt of heparin which was isolated from heparin preparations made from beef lung, beef liver and beef intestine. All these crystalline barium salts are similar in their composition and physiologic potency. Charles and Todd, after careful observations of the chemical behavior of heparin and on the basis of previous work, have concluded that heparin is a mucoitin sulfuric acid in which the fundamental structural unit consists of two molecules of acetyl glucosamine and two molecules of glycuronic acid. Each unit also contains five sulfuric acid groups, which impart strongly acidic properties to heparin; physiologic inactivation follows the removal of the sulfate groupings.

The provision of highly purified preparations of heparin for experimental study encouraged clinical use of this substance. Jorpes has attempted to demonstrate heparin directly in the walls of the large blood vessels by the use of toluidine blue, which stains heparin strongly metachromatically. Within a few hours after large vessels have been immersed in a dilute solution of toluidine blue there results a purple staining of the vessel walls, most marked near the lumen. The old idea that heparin is localized in the vascular system thus appears in a new form. Further study in collaboration with histologists pointed to the mast cells of Ehrlich as responsible for the metachromatic purple coloration obtained with the staining dye. Strongly suggestive proof was then obtained that the granules of the mast cells of Ehrlich consist of heparin. Moreover, a rather good correlation was found between the histologically demonstrated content of mast cells of various tissues and organs and the content of heparin which they yield. There is other supporting proof for the conclusion that the metachromatic granules in the mast cells of Ehrlich consist of heparin. These cells, by virtue of their position around the capillaries and certain of the small blood vessels, apparently have the opportunity of emptying the contents of their granules directly into the blood stream.

The isolation of relatively pure heparin [3] has led to an extensive examination of the relationship of this anticoagulant to the problem of thrombosis, particularly, by Best and his collaborators at Toronto.[1] It was demon-

1. Jorpes, J. E.: Heparin, London, Oxford University Press, 1939.
2. Charles, A. F., and Todd, A. R.: Observations on the Structure of the Barium Salt of Heparin, Biochem. J. **34**: 112 (Jan.) 1940.
3. Heparin is not generally available for clinical use.

strated that heparin greatly inhibits the formation of thrombi produced in animals by mechanical or chemical trauma to the intima of large exposed veins. The ability to produce coronary thrombosis in dogs by means of sodium ricinoleate was also greatly diminished in heparinized animals, as compared to control dogs which did not receive heparin. These successful experiments have stimulated the use of pure heparin in clinical cases of thrombosis and remarkable results have been reported at the Toronto General Hospital and in Stockholm.[3] Heparin has been employed postoperatively with a high degree of success; pulmonary embolism or thrombophlebitis was not observed in instances in which these complications might ordinarily be expected. Although it is somewhat difficult to evaluate postoperative treatment for the prevention of thrombosis, more direct evidence of the value of heparin may be obtained in the treatment of an existent thrombus. Striking claims have been made in the Swedish clinics [1] for the value of heparin in the treatment of thrombosis in the main trunk of the central vein of the retina, and subsequent definite return of visual acuity has been reported. Similar efficacious results with heparin are reported in vascular surgery.[1] In recent preliminary publications in THE JOURNAL,[4] suggestions have been made for the use of intravenous heparin drip, in conjunction with sulfapyridine, in the treatment of subacute bacterial endocarditis. The prevention of embolus formation greatly diminishes the nidus for growth of bacteria and vegetations.

Future clinic work may definitely establish the value of heparin in clinical thrombosis, coronary thrombosis, thrombosis of the large veins and thrombophlebitis. Heparin, like many other therapeutic substances, is the product of the combined efforts and interests of the physiologist, the biochemist and the clinician and has now passed from pure physiology to medicine by way of biochemistry.

3. Murray, Gordon: Heparin in Surgical Treatment of Blood Vessels, Arch. Surg. 40: 307 (Feb.) 1940. Jorpes.[1]
4. Kelson, S. R., and White, P. R.: A New Method of Treatment of Subacute Bacterial Endocarditis, J. A. M. A. 112: 1700 (Nov. 4) 1939. Friedman, Meyer; Hamburger, W. W., and Katz, L. N.: Use of Heparin in Subacute Bacterial Endocarditis, ibid., p. 1702.
1. Fosdick, R. B.: The Rockefeller Foundation, A Review for 1939, New York.

## Current Comment

### THE ROCKEFELLER FOUNDATION

The review of the 1939 work of the Rockefeller Foundation presented by its president, Raymond B. Fosdick,[1] clearly illustrates the interdependence of scientific work throughout the world. Hampered as the work of this foundation now is by factors beyond its control, the report exemplifies the many ways in which expenditures trifling in comparison with armament expenditures can influence the scientific, medical and social lives of vast numbers of people. The work supported by the foundation in South America against the dreaded malaria-carrying mosquito Anopheles gambiae, imported from Africa, represents a campaign the outcome of which is of importance to the entire continents of South and North America. Similarly the studies on yellow fever actively initiated by the foundation as well as numerous other public health activities and assistance in other branches of medical science are of profound importance to the public health. The foundation also gives material encouragement in the fields of natural science, the social sciences, library work, the educational activities of radio, the humanities, health and educational activities abroad, especially in China, and in its assignment of fellowships throughout the world may be serving to keep alive some spark of international cooperation which will help in reconstruction at some later date.

### FOURTH OF JULY FIREWORKS INJURIES

This year the American Medical Association, as in the previous three years, will compile its annual summary of fireworks injuries resulting from the celebration of the Fourth of July. Although several states have adopted effective antifireworks legislation, the injuries in 1939 nevertheless numbered 5,560 and the deaths thirteen. These figures clearly indicate that there can be no relaxation of efforts to prevent such unnecessary accidents. Hospitals throughout the country are therefore again asked to cooperate in filling out the questionnaires which they will shortly receive to list the deaths and injuries from this source.

### FOOD AND DRUG ADMINISTRATION TRANSFERRED TO FEDERAL SECURITY AGENCY

President Roosevelt's Reorganization Plan No. IV, which was commented on in a previous issue of THE JOURNAL,[1] becomes effective June 11. On that day, pursuant to the President's plan, the Food and Drug Administration and its functions, except those relating to the administration of the Insecticide Act of 1910 and the Naval Stores Act, will be transferred from the United States Department of Agriculture to the Federal Security Agency. Thereafter the Administration will function as a separate unit under the direction and supervision of the Federal Security Administrator. The chief of the Food and Drug Administration will be known as the Commissioner of Food and Drugs. On the same day St. Elizabeths Hospital, Freedmen's Hospital, Howard University and the Columbia Institution for the Deaf will also be transferred to that agency. For years the American Medical Association has recommended, and in its Platform it continues to advocate, the establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy. The President's Reorganization Plan No. IV and the prior transferal of the United States Public Health Service to the Federal Security Agency would seem to indicate an attempt by the President to gather together under one agency the diverse medical and health functions of the federal government.

1. Reorganization Plan No. IV, editorial, J. A. M. A. 114: 1561 (April 20) 1940.

# ORGANIZATION SECTION

## VOLUNTARY HEALTH INSURANCE IN THE NETHERLANDS

MOLLEURUS COUPERUS, M.D.
CHEHALIS, WASH.

During the summer of 1939 Dr. J. J. Couperus of Rio Vista, Calif., and I visited the Netherlands and while there investigated the system of voluntary sickness insurance which is in operation there. We received hearty cooperation in the accomplishment of this task from the officials of the Association for the Advancement of Medicine in the Netherlands, the official medical organization of Holland.

Prior to 1912 the business of offering sickness insurance to the low income class of the Netherlands was entirely in the hands of private and mutual insurance companies. There was a deplorable lack of cooperation and understanding between the various groups interested in this insurance, and conditions gradually became such that the medical organization of the Netherlands decided to take the leadership in solving this important problem.

In 1912 the Association for the Advancement of Medicine succeeded in unifying sickness insurance by drawing up a plan for an acceptable health insurance policy. Private companies who adopted the suggested policy could be endorsed by the association, and in addition the association established a sickness insurance company of its own. The insurance policy as recommended to the private companies was identical with the policy of the insurance company fostered by the medical association. Since the year of its inception there have been many changes in the original plan, but in the end this plan of voluntary sickness insurance for the low income group has become an integral part of the life of the people of the Netherlands.

### GOVERNMENT SEEKS CONTROL OF INSURANCE PROGRAM

In 1925, when a cabinet that was socialistically minded came into power, the government of the Netherlands made an attempt to gain control of the sickness insurance program. After investigation, however, it was found that the administrative expenses, which had been, and still are, from 8 to 10 per cent of the total receipts, would be increased about fourfold when in government hands. Consequently the plan was abandoned and the medical association continued to regulate the health insurance business. However, the government has its independent industrial accident insurance. The low income insurance plan does not treat any sickness which would fall under government industrial accident insurance.

Of the eight million population of the Netherlands, four million, or 80 per cent of the low income group, are voluntary subscribers to this health insurance plan. One and a half million of these are insured directly by the medical association, while the remaining two and a half million are insured by private companies endorsed by the medical association. There are 4,200 practicing physicians in the Netherlands, and more than 4,000 of these have voluntarily enrolled with the medical association to serve on this insurance program. When a physician decides to participate in the plan he applies to the nearest insurance office; his application is acted on within a month, and if he is a member of the medical association he is accepted. If he is not a member, it must be established that his professional conduct is above reproach. However, at present all practicing physicians in Holland are members of the medical association, in spite of the fact that the annual dues amount to 60 guilders (about $32). After the physician has been placed on the roster of insurance physicians he is given a list of the insured who have selected him as their family physician. The average number of patients a physician has on his list usually does not exceed 1,750. The maximum number of individual patients on any physician's list, except under very unusual circumstances, may not exceed 3,000. For those patients who are on his list, the physician receives a minimum of 3.50 guilders ($1.85) per individual annually, payable quarterly. Physicians who live in the country are allowed 5 or 6 guilders ($2.65 or $3.18) a year per patient; extra mileage and the furnishing of drugs to the patient accounts for the difference in the fee. The physician has practically no report blanks to fill out concerning his patients. Specialists are paid according to a special fee schedule previously agreed on between them and the insurance company.

Any one who has an income of less than 2,100 guilders ($1,113) a year if single or 3,000 guilders ($1,590) if the head of a family, may enroll as a subscriber to the sickness insurance plan for the low income group. The insurance fee for a single individual is 25 cents a week. This entitles him to professional care by his family physician, the services of a specialist when ordered by the general practitioner, surgical treatment, x-ray service, laboratory work, drugs, ambulance service when required, and the use of such medical and surgical appliances as may be needed, including wheelchairs and crutches. For an additional 8 cents a week he is also insured for hospital expenses (ward accommodation) for a period of six weeks; by paying a slightly higher fee he may obtain complete hospital coverage for an indefinite period. There has been a definite tendency on the part of the insurance company to supply only the latter type of hospital insurance. The cost of complete medical and hospital insurance for a family of average size is about 90 cents a week; as soon as a child reaches the age of 16 the parents must pay a separate fee for that child. Those who have a chronic or recurrent illness before joining the insurance plan must pay a higher fee than if they were in normal health. Obstetric service is included in the plan, but there is a short waiting period before this part of the insurance becomes effective, and the insurance premium is slightly higher during the months in which the woman is pregnant. Eyeglasses are furnished only once in two years on the prescription of a physician.

The country is divided into some sixty insurance districts, corresponding quite closely to the areas of the local medical societies; each district has its own board of physicians and lay members. The insurance premium is collected each week by salaried messengers.

This insurance plan for the low income group in the Netherlands may be called a distinguished success. With only one exception, all physicians whom we ques-

tioned heartily endorsed the plan. They felt that the position of the physician was improved with regard to working conditions as well as to payment for services rendered to those in this group. They also stated that the low income group received better medical care than it had before the adoption of this plan. One physician, who was a specialist in internal medicine and not an insurance physician, stated that he believed that the number of patients allowed per physician should be smaller and that the physician's fee per patient should be larger. When we asked the patient about the insurance scheme we found undivided and enthusiastic support of the plan. At the headquarters of the Association for the Advancement of Medicine the opinion was given that the plan has worked well for all concerned, and the results of our investigation supported that opinion.

An insurance plan to cover those of larger incomes, the middle class, had been in preparation for a number of years and was ready for operation in the fall of 1939. Those whose taxable income does not exceed 4,000 guilders ($2,120) a year for a single individual or 5,000 guilders ($2,650) for a family may join this plan. The insured receives the services of his family physician, a maximum of ten calls a year at a specialist's office, hospitalization, drugs, ambulance service, and the use of clinical laboratories (including x-rays) but not dental care or obstetric service. However, after one year of membership, surgery necessitated by pregnancy is allowed, such as cesarean section or surgery for rupture of the uterus. For this insurance the patient pays an enrolment fee of 1 guilder (53 cents) and an annual basic contribution of 50 guilders ($26.50) for a single male, 60 guilders ($31.80) for a single female, 84 guilders ($44.50) for a man and his wife, 110 guilders ($58.30) for a family with one child, 135 guilders ($71.55) for a family with two children and 15 guilders ($7.95) for an additional child; these fees are payable in advance in monthly instalments. After one has joined the insurance plan there is a waiting period of three months, during which the insured must pay his own medical bills; the insurance premium paid during that period is placed in a special fund to the credit of the insured. After the waiting period is past, all medical bills which the insured incurs are forwarded by him to the insurance office, which pays the doctor, druggist and hospital. To counteract the tendency to seek unnecessary medical service, part of the annual premium is put to the credit of the insured in a special fund. If the medical bills remain below two thirds of the annual premium, whatever amount is left of the premium will be added to the personal reserve fund of the insured. When this fund contains 100 guilders ($53) interest is paid on it; when it reaches the figure of the annual premium the excess is deducted from the next premium. Should the insured decide to discontinue his sickness insurance policy, the money in his personal reserve fund will be returned to him by the insurance company. If, during any year, the medical bills of the insured exceed his premium as well as his reserve fund, he is expected to pay a small percentage of this excess amount. For example, should the medical bills for the year reach 300 guilders ($159) the insured pays an extra assessment of 16.50 guilders ($8.75) above his basic annual premium. If his medical bills should total 1,000 guilders ($530) he must pay an extra 79.50 guilders ($42.15). Thus the insured has a perpetual interest in keeping his medical bills at a minimum.

Under this plan of sickness insurance for the middle class the physician is paid his customary fee for private patients. The physician sends an itemized statement to the patient, who has an opportunity to check both the services rendered and the fees charged; he must forward the bill within a month to the insurance office.

The insurance company of the medical association also is planning to take over the medical care of the destitute. In the past these unfortunates have been cared for by physicians who entered the lowest bid to the city or county for the medical care of their poor. Under the new plan the city or county pays the insurance company for each patient a premium slightly less than what is paid by other members of the low income group insurance plan. For this the poor man receives complete medical care and has free choice of his physician. It is expected that the plan will please the city and county governments, the patients and the medical profession.

1037 Market Street.

---

# NATIONAL CONFERENCE ON MEDICAL NOMENCLATURE

**Held in Chicago, March 1, 1940**

**DR. HAVEN EMERSON, New York, in the Chair**

*(Concluded from page 2029)*

### The Classification of Tumors for Clinical Purposes

DR. BOWMAN C. CROWELL, Chicago: The present report of the committee is labeled a progress report but the committee was appointed only in January and it has not been possible to have an assembly of the members as yet. Therefore the present report of progress must be interpreted as a report by the chairman of the committee, who has as yet received help from only a part of his committee.

Neoplasms have been classified from many standpoints: etiology, clinical features, histogenesis, embryology and gross anatomy. No terminology that can be devised in this field will meet with approval of all workers in tumors, but the committee has in mind the objective of compiling a nomenclature which will best serve to correlate for statistical purposes the known clinical facts concerning tumors. The classification should be usable by clinicians, but this statement recognizes the frequent dependence of the clinical practitioner on the pathologist. Gross anatomic features of a tumor cannot serve as the only basis for classification and yet they cannot be entirely neglected. It does not seem possible to compile a satisfactory terminology based on any one feature of tumors, and the best that can be hoped for is one that will portray as well as possible the present known facts on the subject. It is proposed to place anew before the members of the Committee on Nomenclature of Tumors a full statement of the individual problems with which we must deal and, from the responses, compile a semifinal report for the members of the committee to consider again.

It will be necessary to enter into some of the details of the task:

1. The question has been raised as to whether the nomenclature should include in the body of the book a list of the complications that arise from neoplasms. It is proposed that the principal of these complications should be listed under 800 "Structural or Functional Changes Due to Neoplasm" and should not appear except by number in the body of the book. They should appear in the index.

2. To cover rare tumors in unusual locations it is suggested that only the more common tumors be listed in the body of the

book under the individual organ and that for the rarer tumors the list from the revised etiologic classification be recommended.

3. Numerous examples of the listing of mixed neoplasms occur in the present edition. Most so-called mixed tumors are not mixed tumors in the sense that they are of teratomatous origin. This applies particularly to those tumors which may contain cartilage or bone, or a fibroma containing fat. All such tumors should be deleted. The teratomas should be retained and perhaps the term "mixed tumors" in the case of the salivary glands when the name has a clinical connotation of some importance.

4. Shall four digits sometimes be used to indicate a modification of a particular variety of tumor? For example, pigmented basal cell carcinoma of the skin. The majority of the committee believes that three digits can sufficiently describe a tumor. Such a recommendation recognizes the desirability of three digits for the use of those who employ the punch card system of tabulation and also the fact that individuals engaged in special research can amplify the system to meet their own needs.

5. Suggestions for changes have been made in the case of tumors of the nervous system. For example, it has been suggested changing capillary fibro-epithelioma to craniopharyngioma. There is considerable objection to giving topographic names to tumors.

6. The committee has been asked to consider the use of the term "syncytial endometritis." I mention this because it involves certain policies. Such a condition is inflammatory, but a true tumor in the form of syncytioma may arise. This tumor should be recognized under 798-889. If it is purely inflammatory it may appear as 794-614 Retention of Placental Fragment.

7. The term "transitional cell carcinoma" appears in the body of the book in previous editions. If this term is to be retained, it should be applied only to tumors arising in areas where transitional cells normally occur, which is not the case at the present time. Many, if not the majority, of the so-called transitional carcinomas are modified squamous cell tumors and should be so listed.

8. In reference to the subject of pigmented tumors it will be profitable to avoid discussion of histogenesis and be content with the term "malignant melanoma," which cannot be a subject of controversy.

9. There is some lack of consistency in the present edition in dealing with neoplasms arising from the fetal anlage. It is proposed that the list under section C on page 87 be enlarged to include the known instances of this entity. They could well be placed under 87x.

10. It has been interesting to note the unanimity of members of the committee to the suggestion that the term "hypernephroma" be deleted. It has served as a cloak for much ignorance. When these tumors arise in the kidneys they should be classified as carcinoma of the kidney and, when in the adrenal, they should be classified as adenomas or adenocarcinomas of the adrenal cortex.

11. Glomus tumors should be recognized and given an appropriate place in the etiologic classification. Any alleged relation of this tumor to Schimmelbusch's disease should be completely ignored.

12. It has been suggested that adenocancroid of stomach and intestine should be recognized. A final recommendation as to the disposition of this entity is reserved for the future.

13. Endothelioma is a term which has served as a catchall for many tumors the nature of which could not be accurately determined. A recommendation will be made later, but the term should be retained in the etiologic classification and referred to under a certain group of organs.

14. With regard to muscle tumors several members of the committee feel that introduction of the term "myoblastoma" would be confusing and is a reversion to the time when every mesodermal tumor was supposed to have arisen from a specific cell. Most of these tumors are leiomyomas. The fibrous element in them is apparently not neoplastic. We suggest the retention of the term "myoma" with the subheadings of leiomyoma and rhabdomyoma when their origin from smooth or striated muscle can be determined.

The personnel of the committee is Dr. A. C. Broders, Rochester, Minn.; Dr. C. L. Connor, San Francisco; Dr. Max Cutler, Chicago; Dr. C. F. Geschickter, Baltimore; Dr. Ralph E. Kendall, Hartford, Conn.; Dr. L. A. Pomeroy, Cleveland; Dr. Mont Reid, Cincinnati; Dr. Walter Schiller, Chicago; Dr. Shields Warren, Boston; Dr. John E. Wirth, Baltimore, and Dr. Bowman C. Crowell, Chicago, chairman.

DISCUSSION

CHAIRMAN EMERSON: Is this, in the main, the way you wish to have the revision undertaken, by specialist committees nationally representative, to take up each of the moot problems within individual specialties? This is a sample of the kind of thing that is in process and that must be done over the ensuing months.

DR. GEORGE BAEHR, New York: The plan for this Committee on Tumors and for other committees seems perfectly feasible. It would seem wise to have representation of national organizations designated to work with the committee. Although the national society should be sufficiently represented, there should be some authority given to the special committee to make recommendations to the central group that assists in the final preparation of the revised edition.

DR. MORRIS FISHBEIN, Chicago: From the point of view of getting the job done, and getting it done with the utmost usefulness at the end, there are two points that should be kept in mind: First, that it is hard to get people to do this kind of work. People here represent an especially interested group, but the number of men sufficiently interested to give largely of their time and of their effort is not so great as to provide a wide latitude of choice. I agree with the suggestion of Dr. Baehr that it will not be possible to organize committees on a strictly representative basis, including all national organizations, and then to expect appointees from those committees to carry back the discussions to the organizations. That method would carry on the work interminably and we would never get anything done. The second point is that it is of the utmost importance that we approach this with the philosophy again in mind that we are not going to make all the changes that we could make. We know that medicine advances rather rapidly and that specialists frequently have concepts regarding the uses of such material which are far beyond the practical application of those concepts by the vast majority of hospital record librarians and clinicians in hospitals that will use the Standard Nomenclature. It is quite possible to take up any one of these classifications and make innumerable changes, just because a change is possible. On the other hand, as Mrs. Walker pointed out, it is rather important not to change too rapidly, not to change before it is certain that the change is one which will stand, so that one will not have to be constantly shifting the code numbers and the use of the book.

## AFTERNOON SESSION

CHAIRMAN EMERSON: The four departments of the government have not found it practicable to use the Standard Nomenclature. We know the difficulties and limitations of material they handle in their respective institutions, but an important gesture that we should look forward to is an agreement among the federal departments either to accept or to improve what is acceptable generally to the institutions for the sick elsewhere in the country. Each one of these departments deals with the other department's patients at one time or another, and the interchange of cards and records causes duplication and confusion which might be avoided if this Standard Nomenclature were used by all the federal departments. I hope the representatives of the four federal departments here will see if they can't come to an agreement, so we can deal with them as a unit instead of four different hierarchies of medical practice.

### Progress Report on Revision of the Standard Classified Nomenclature of Disease

DR. EDWIN P. JORDAN, Chicago: We have received in this office a large number of letters from record librarians, physicians, and hospitals and other groups calling attention to specific omissions or mistakes in the Standard Nomenclature, criticizing the Standard Nomenclature in certain respects and making suggestions. For the most part the suggestions have been divided much as the book has been divided, into the special sections in which they properly belong. Some of them are matters of general editorial policy. The mechanism of action has been to

place these suggestions in the hands of individuals who had previously been interested in the Nomenclature, or other individuals or delegates of special societies who were especially interested in classification in their respective fields. After referral, we received comments as to whether changes should be made, additions made, or deletions. There has been much more pressure for additions than there has been for deletions. At present this revision is far advanced. Practically every section has already been subjected to careful examination both in this office and by specialists, and most of the proposed additions have been either rejected or accepted. There have been changes made where indicated, and a few deletions. We should at this time recommend some mechanism for approving or disapproving the specific sections of the Nomenclature. The revision of each section but two has been practically completed, so that we have made the changes on the particular pages to which they apply.

It is believed that there are many places in the Nomenclature which can be simplified and that some of the requests for additions should be resisted, but that nevertheless the Nomenclature can be complete from the standpoint of classification. An important question is How often will it be necessary to revise the Standard Nomenclature? What is the feeling of the conference? Related to this is the question whether it would be possible to develop supplements to go out to the purchasers of the Standard Nomenclature at intervals of an unspecified number of years rather than such frequent complete revisions of the Standard Nomenclature.

The whole question of the formation and mechanism of action of special committees might be discussed at the same time. It is almost certainly advisable that there be some kind of permanent editorial committee to discuss or to consider questions of editorial policy arising in the intervals between the national conferences on medical nomenclature. Other committees are probably indicated. The approval of the work of the special committees or special sections of the Nomenclature is rather important. Is it going to be necessary to require or to obtain the approval of national specialists' societies on particular sections of the book? The mechanism of doing so would be awkward. There is a delay between the time when revision is complete and the time when it would come before an annual meeting of a large specialist society. The formal action of the society would ordinarily add little to the book itself, since work of this kind is generally done by one or two individuals in each specialty, anyway.

DISCUSSION

DR. THOMAS R. PONTON, Chicago: I think the Nomenclature should be revised at least every three years. There is a constant change in the terminology of medicine, and if we are going to keep up to date we must make provision for revision. I see no reason why we should not adopt a loose-leaf system of publication. The idea of a pamphlet revision is impracticable. With the Alphabetical Nomenclature, at one time revision became necessary after publication of our first bound volume. We did not want to put the people in the hospitals to the expense of buying an entirely new Nomenclature, so we published a pamphlet revision. We even went to the trouble of publishing that on a paper that could be cut and the revisions pasted in as marginal notes on the original edition. In my visits around hospitals I never saw one of those used. That revision was not worth the time and expense of getting it out. The loose-leaf, however, I believe practical. We can then, at intervals of three years, publish supplementary pages which will replace those already done. In that way, without the hospitals going to the expense of buying an entirely new volume, they will be up to date. It is surprising to find hospitals today using some of the old nomenclatures. I ran across a copy of my original Nomenclature published in 1927, in visiting a hospital two years ago. The statement was made that they didn't feel justified in buying a new Nomenclature to put on the several floors of the hospital. That is the reason I believe in the loose-leaf idea.

DR. GEORGE BAEHR, New York: The question of a loose-leaf volume was considered when the previous editions were published. A preliminary trial printing of a Nomenclature was made in 1932, and after about a year when many of the omissions were picked up the first official edition appeared, in 1933. However, after hospitals began to use it a great many more omissions and inaccuracies were discovered, and it became necessary to publish the second—this is the last edition—in January 1935. So it is now more than five years since this edition was printed. From the fact that our attention is being called to fewer serious omissions, we can safely put off publication of the new edition for probably ten years, provided, the new information that may arise, or new designations in disease that may be decided on, be called to the attention of hospitals that have subscribed, in some way, either by a supplementary pamphlet issued every few years or by some letter form that can be used in the record room and in the wards for making proper corrections in the book. I am in favor of a ten year revision, with supplementary information distributed when necessary during the ten year period.

DR. MORRIS FISHBEIN, Chicago: We in the Association office will be largely responsible for the entire printing task and the upkeep and maintenance of the organization necessary to carry this work out. The matter of a loose-leaf system is almost out of the question because of the difficulty of developing such a work, the increased cost and the cost of maintenance. While hospitals might object to buying a new edition, the initial cost and maintenance on loose-leaf is considerably greater than the publication of a single volume. The frequency of revisions must be intimately bound by the mechanism by which the revision is to be brought about. We should first address ourselves to the question as to who is to undertake the primary responsibility for the publication. One of the first steps is to select some one who will act as chief editor of the publication and carry the final responsibility. The Board of Trustees of the Association, at the suggestion of the General Manager and the Editor, has selected Dr. Jordan to take that responsibility. The next question relates to making the final decisions in each field. Obviously we must have committees. These committees cannot meet every month or even every year to go over the entire question of changes in nomenclature and will have to consider by correspondence the suggestions that are made. Then, as each member gives his opinion, it will probably be up to the chairman of the committee to make the final decision as to the necessary revisions, based, of course, on the information sent to him by the members of his committee as to what changes are to be made. His committee, having made that decision, will forward its corrections to Dr. Jordan, who would then arrange for proper incorporation of those suggestions into the volume. Should he find it undesirable to incorporate the changes voted by that committee, he would have to refer the matter back to the committee for further consideration. It is the desire of the American Medical Association to have this Nomenclature a cooperative effort in which all the learned societies and all those having responsibility in this field will indulge, and that means there must be conferences. The Board of Trustees decided that a conference about every five years, of this type, would serve to crystallize the points of view of those most interested. In other words, each five years a conference of this type might be held, the opinions that had developed in the meantime crystallized, committees to carry on the work until the next conference established, and a revision of the book brought out. That would not necessarily mean that each hospital would have to buy all new books every five years. It should be possible to develop in small pamphlet form the essential changes, so that those hospitals which did not care to invest in a new volume could buy the pamphlet containing the fundamental changes that had been made in the five year period. That is a compromise between the issuing of annual or monthly, semiannual or biennial supplements and the loose-leaf system. I am trying to be practical in keeping the cost of the work down to a minimum in order to get the widest possible use. If we would adopt a procedure whereby we would issue the book at about five year intervals we could keep it at the present relatively low cost. Then the hospitals could decide at each five year period whether or not to invest in a new edition or to invest in a book of revisions, for which the record librarian would have the responsibility.

CHAIRMAN EMERSON: The policy which we found indispensable in the years we were carrying it on in New York was that there had to be an executive committee of the National Conference that met several times a year to confer with the editor on

matters of general policies which were presented to us by the conflicting interests of the specialty groups we had asked to advise us. We may find a similar method desirable in addition to the special subcommittees. The specialist subcommittees should have indigenous authority, as it were, to express preference for or against inclusions of changes.

DR. MONTAGUE L. BOYD, Atlanta, Ga.: Is it essential that a definite time be set for revision?

CHAIRMAN EMERSON: Every ten years we must look forward to the decennial revision of the International List of Causes of Death. That is a thing fixed, after sixty years of practice among the nations. We are dealing with matters that change much more quickly and that are subject to clinical fashions and the influence of university teachers and hospital leaders. If we could commit ourselves now to an edition in 1945, the one that comes out in 1950 will be the one that will immediately follow or be almost coincident with the international revision of that year, which will, in fact, take place in the year 1948.

DR. BOWMAN C. CROWELL, Chicago: I would like to move that this conference go on record as recommending to the American Medical Association a consideration of a quinquennial revision of the work.

DR. EDWIN P. JORDAN, Chicago: Before passing the motion I would like to hear from the record librarians.

MRS. STELLA FORD WALKER, Chicago: The record librarians are not the ones to fix a policy of that sort. I have used the Standard Nomenclature only three years and I have had few requests in that time for questions of extension of the code that we couldn't take care of without upsetting any of the other questions. There have been occasions when the specialties have wanted additional items in their sections, but we found ways to take care of it. A five year revision is all right, as far as my experience goes.

MISS DOROTHY L. KURTZ, New York: A five year revision would be what I would suggest, from a record room standpoint.

MISS LILLIAN H. ERICKSON, Chicago (American Association of Medical Record Librarians): I think the five year period would take care of the medical record librarians. The record librarians would be happy to be represented on the Advisory Board and possibly bring forward some of their problems, as far as usage of the Standard Nomenclature is concerned.

DR. NEIL A. DAYTON, Boston: We already had the old classification on our statistical cards in 1933, and we had to change over to the new nomenclature at that time. It cost us in our department about $600 to change over the cards for our resident population. If that were happening any oftener than every five years, it would be quite a little expense. I think five years is the ideal period.

COL. CHARLES G. SOUDER, Washington, D. C. (United States Army): Our nomenclature in the Army, which is quite a restricted one, has not been materially revised since 1917. If you want to use statistical material for purposes of comparison, I should think the more stable the Nomenclature could be and the less frequently revised, the better it would be. I would suggest a revision coincident with that of the International List of Causes of Death, not oftener than every ten years. There will be, of course, a great many changes, but will it not be true that those will be changes in diseases of infrequent occurrence, so that the necessity for any elaborate change should not be great? Medical knowledge is not going to increase at that rate. Medical fads and fashions will change, but I don't think they should be given undue attention.

CHAIRMAN EMERSON: Isn't it true that the list used in the Army is much more restricted in number, and isn't it inevitable that a list that decides to restrict itself in the beginning is likely to have less demand for change than one which is as comprehensive as the one we have attempted?

COLONEL SOUDER: Our list of diagnostic terms is limited to 1,000. If the physician wants to call tonsillitis something else, we tell him he can't do it.

CHAIRMAN EMERSON: And the Public Health Service Nomenclature is 10,000.

CAPT. WILLIAM E. EATON, Washington, D. C. (United States Navy): The current Nomenclature of the Navy, which was just issued in our new manual for 1939, contains 2,715 diagnoses, which are classified under various groupings, there being twenty-seven classes. This has about the same categories as the Army list. We take into the hospital the Navy and Marine Corps men, the Army men from Fort Sheridan and, when necessary, elsewhere, the Civilian Conservation Corps men up to the number of sixty, the WPA workers and some veterans. Our diagnoses are satisfactory to all these agencies. We have the Veterans Bureau list which we use also. The Navy is a highly specialized service. We find conditions that may not occur in civil practice. We have to fit the diagnosis to the condition. From time to time we find additional diagnoses which we have to put in to have something to use in connection with some of the features of naval affairs. I have tabulated things under injuries and under the various causes of violence. In aeronautics we have collisions in full flight with other aircraft, collisions in full flight with objects other than aircraft—such as running into a boat on the water. We have to conform to this restricted list. Reports go into the bureau and are put on the tabulating machines. We can tabulate diagnoses and obtain statistical data by just asking at the door of the room where it is done. We have a stated number of operations which take up about four pages of our pamphlet, in English, in Latin and in anglicized Latin, which fulfil our needs. If any interested individual would show the Surgeon General of the Navy a need to add to or change, I think it could be done with cooperation.

DR. HOWARD FOX, New York: There are two questions: first, what we want, and, second, will the American Medical Association finance a revision every five years? I think five years is an ideal time for such an extensive book.

CHAIRMAN EMERSON: It is curious that a man in the Army can have only 1,000 sicknesses, and when he is in the Veterans Bureau he can have 15,000, and when he comes into the clinical care of clinicians in civil practice 1,000 isn't nearly enough to specify the kinds of things he can have. It isn't a question of recommending to the Navy that they have the same number of diagnoses that we have, but to suggest the desirability in comparability of professional accuracy and completeness of description of both etiology and location. Those are things which we believe the federal medical services might with advantage study, to see how nearly they can come up to the degree of precision and completeness which has been found desirable in systems with a great many more hospital beds, even, than those that are represented in the federal service. The motion is that there should be a revision every five years and that we ask the American Medical Association to commit itself, so far as possible, to that policy. Those in favor of this policy please may "aye": opposed, "no." I hear no "noes," and the resolution is passed. The other matter is, Shall we suggest the creation, under the editorial policy of the American Medical Association, of a general advisory committee on editorial policy to act, as it were, as an executive committee in the interval between the quinquennial conferences?

DR. FISHBEIN: If this conference were to recommend to the Board of Trustees of the Association a suggested editorial board the Board of Trustees would probably accept the suggestion. I move that there be developed an advisory editorial board of six to cooperate with Dr. Jordan, as managing editor of this publication, with a view to serving during this next five year period as an advisory editorial board for the publication of the Standard Nomenclature, and that it be left to the chairman of the conference, with the executive committee that was established in the original conference, to nominate to the Board of Trustees of the Association the members of the advisory board of six.

[The motion was seconded and carried.]

CHAIRMAN EMERSON: The appointment of the subcommittees was proposed in the same manner, or would those subcommittees be appointed by the editorial committee?

DR. FISHBEIN: That is for the conference to decide.

CHAIRMAN EMERSON: We should leave the appointment of the special subcommittees, as may be needed, to the editorial committee.

DR. DUNN: Since I have been in this conference I have heard of at least two lists I didn't know about, one of diseases and one of operations. I think Dr. Jordan would do a good service if

he could list the terminologies that are being used so that all of us could write and get them and see what they are.

DR. BAEHR: Miss Kurtz has made a suggestion concerning necessary abbreviation of the Standard Nomenclature which must be taken seriously because of her large experience and her deep interest in this subject. However, what abbreviations are made cannot do violence to the basic plan or require any radical changes in the record room filing. Otherwise, in attempting to solve the criticisms and objections of one group, one will lay oneself open to a tremendous wave of criticism from all the hospitals that will be inconvenienced. However, the volume can be reduced in size. Also in some parts of the book some of the headings can be put in boldface type and can be employed by some of the special services which do not want to keep a record of the refinements in the categories under the main headings. I refer, for example, to a condition like obesity, which diagnosis will be adequate for a surgeon but might not be adequate for an internist, who might want to group his cases of obesity as due to overeating, to hypothyroidism and to other causes. Similarly, under tetany somebody might be quite satisfied to put down the term "tetany" and let it go at that. It isn't a complete diagnosis, but no one can force a clinician or a specialist to go into refinements of diagnosis if he is incapable of doing it or if he doesn't want to do it. However, under tetany one will find that there are six or seven types and different types of mechanism, and for those who wish to record the different varieties the volume should permit that and yet, at the same time, allow flexibility. I think that this can be accomplished without doing any violence to the basic philosophy underlying the work.

MISS KURTZ: The main point I wanted to bring out this morning has been rather obscured by what was merely a suggestion. The abbreviated list was the suggestion, and not the main point. What we wanted to make sure this conference would consider was the difficulty that one group of specialists found in dealing with terms that belonged to another group. We wanted to make sure that some provision was made by this conference to look into that matter, and not merely treat it, as has rather been the habit heretofore, as just a lazy man's excuse. We think it has got beyond that point.

DR. WARREN P. MORRILL, Chicago (American Hospital Association): If Columbia-Presbyterian, with its staff, finds difficulty, how much is it multiplied in the general run of nonteaching hospitals? I suggest that there be in the actual format this distinction between obligatory and voluntary terminology; that is, "obesity," which may be sufficient, would be an obligatory term perhaps printed in boldface type, with the subdivisions under it. The seven migraines could be left for those who are interested in the distinction between the seven different migraines, while the average man would be obliged to go as far as saying "migraine" but no further.

CHAIRMAN EMERSON: I must reinforce, as a member of the faculty of P. and S. the insistence of my colleagues that we make some move which will permit either a distinction between obligatory and facultative, so that people who wish a simple skeletal scheme of terms can use it without damaging the complete list, which we hope always to have published in toto. There doesn't seem to be any technical reason why that can't be done, and when the committee is ready to consider it I shall be glad to submit from technicians with whom I have been in conference a possible mechanism by which this can be done.

DR. FISHBEIN: It would be possible, after we have had some experience getting out this new revision, to prepare as a simple pamphlet a list of the main headings and subheadings with the numbers, for the use of those smaller institutions which cannot go much beyond that, but such an activity is directly opposed to progress in educating physicians to endeavor to make really descriptive, scientific diagnoses. I think the general effect for the advancement of medicine is vastly improved by endeavoring to hold to the list as now constituted and not to offer a short-cut simply because that is cheaper and easier.

DR. BURRILL B. CROHN, New York: The diseases of the alimenary tract constitute sixty-nine pages of this book, or practically 15 to 16 per cent of all the terms. Although I sat with the original committee, I am rather annoyed to see how often the same term springs up: achlorhydria, achylia gastrica, hypochlorhydria and acidity, as well as paralytic ileus, and any other number of names. I think, that with authority, I could cut down this one section alone and condense the whole thing into sensible terms and cut the expense of the publication, but I do not think revision of the book should go longer than five years. Five years ago there was no flexible gastroscope used in this country. Today there is a huge terminology and literature growing up on the subject of gastritis, for which there is no provision in the book. If you wait ten years, the subject would probably be obsolete and completely changed before one had a chance to present it. I favor this movement to cut down the size of the book, to simplify the items and stop the duplication of terms. As far as any specialty is concerned, we have no trouble at all with the national society. I have full authority to act or make changes such as I have wished to. I have submitted my report to them. I think a simple committee, working with the approval of the national society, would be a perfect mechanism for the revision of the book.

CHAIRMAN EMERSON: The idea has been suggested that while we continue in the book all legitimate subdivisions of site and etiology which add to the precision and completeness of diagnoses, we make it possible, by some particular selection of printing or order or line of the presentation, to use the frequently employed diagnoses without any necessity in all instances of using the ultimate refinement. If a hospital wants to limit to a certain number instead of going to an ultimate subdivision, it should have the privilege of doing it, but it should do it in a methodical way. We have received practically a self-denying statement from the gastro-enterologist. We may find other specialties will be willing to limit the number of diseases which they recommend that can really be accurately distinguished one from another. That is the first kind of concentration or elimination. It has been suggested that this matter be referred to the editorial advisory committee. Unless I hear objection, I will consider that this matter of abbreviating or abridging or concentrating the list, in any way consistent with keeping the present plan of thoroughness, shall be referred to the editorial advisory committee.

[The motion was carried.]

DR. JORDAN: We have been subjected to many letters and pressures of various sorts to add to the Standard Classified Nomenclature of Disease special diagnostic categories for the classification of dental diseases, pathologic specimens, x-rays, electrocardiograms and others. I feel that this should not be done, that it does not come within the scope of the Standard Nomenclature to include such things, and that there would be no limit to what we would be supposed to add under those circumstances. There are some eight or ten suspected diagnoses in the Standard Nomenclature now. I believe they should be removed. I don't believe the Standard Nomenclature should differentiate between a diagnosis and a suspected diagnosis. If any one wishes to indicate that something is suspected, he can add a Y at the end of the classification. Dr. Baehr referred to one method of simplification which seems practicable and will materially decrease the size of the book. That is the question of listing, as a general diagnosis, certain disorders which may appear in almost every region or organ. An abscess, for example, may appear almost anywhere, and rather than listing it under each organ in which it might appear, I believe we can have a general diagnosis of abscess, with permission given to the physician or the record librarian to fill in the location from the topographic numbers in the book. That would apply to such conditions as abscess, endometriosis, leukoplakia, anthrax, filariasis and many others. They might also be listed and should be listed under the sites where they appear most commonly. Dr. Crowell mentioned the question regarding the listing of complications of neoplasms. We have in the book a number of complications: "perforation of the stomach due to contiguous neoplasm"; "hemorrhage of intestine due to contiguous neoplasm." I believe they should all be entirely removed from the book. The disease is the neoplasm; the rest is a complication. We must realize that some things have to be left to the patient's chart itself. Not every detail of a clinical examination can be placed in the diagnosis. The editorial matter which I wish to bring to your attention is with regard to the use of eight and nine digit diagnoses. It is possible to place such lengthy diag-

noses on punch cards and the question has arisen as to the possibility of making all the diagnoses in the book ten digit diagnoses. On the whole, I think it would be advisable to keep the number of digits as few as possible, but we have received many letters on that subject.

MR. RICHARD H. DYER, Washington, D. C. (International Business Machines Corporation): I was invited to this conference as a representative of a tabulating machine corporation, but I speak in the interest of Dr. Bullock of the Los Angeles County Hospital. The subject he brings up is this, that the number of positions in the morbidity code should be, if possible, reduced to the smallest number. If you will look at the code Mrs. Walker has, you will notice that it has twelve possible positions, and that would indicate, on the basis of the decimal system, that there would be one trillion possible types of morbidity. Using that as a possible index, conceivably there could be some reduction in the number of digits which are used to express any type of morbidity. Another point Dr. Bullock would like to make is this: Since there are probably not one trillion types of morbidity, it might be possible to go to a ten digit code. In other words, our dollars and cents are expressed in ten digits, from 0 to 9. The Logie code is expressed in twelve positions at this time, X and Y. Since scientific agencies throughout the world are using the ten digit system, wouldn't it be possible to revise the code and put it on a decimal basis rather than use a duodecimal or twelve position code? That would simplify mechanical tabulation and make possible certain correlations which are not practical on a machine basis now. Dr. Bullock would also like to see the code established as a fixed unit. In other words, instead of having 3 and decimals added up to a total of six positions, would it be possible to reduce that to five and have it expressed as a five digit code in the Nomenclature opposite the type of morbidity? As a representative of a company in the tabulating machine business, I wish to say that our engineering forces are at work developing equipment which will handle all these problems which hospitals have in connection with their morbidity tabulations.

DR. DUNN: Wouldn't it be advisable to take all the record librarians who are in hospitals that have been actually using this code and solicit from them a complete description of what difficulties they have had in adapting it, the feelings of their staff, and all of the suggestions that must have been cleared largely through them? That would get the practical problems which have been coming up here before the committee.

DR. JORDAN: We have had requests to include in the Standard Nomenclature dental terminologies, terminologies for the classification of pathologic specimens, electrocardiograms and x-rays.

DR. FOX: I move that the requests be disapproved.

DR. FISHBEIN: On the ground that it is not feasible, with the present setup, to take up such extra sections as are requested. It is not expedient at the present time to undertake them.

### Problems of Terminology in the Field of Physical Medicine

DR. FRANK H. KRUSEN, Rochester, Minn.: I appear as a representative of the Council on Physical Therapy and as chairman of its Committee on Nomenclature. We are interested not in statistics but in preparing a workable classification of therapeutic procedures in the field of physical medicine. Our problem is to obtain a list of definitions. We have tried getting the written opinions of a large group of specialists, selected because of their locations in leading hospitals and institutions. The plan was not particularly satisfactory. We then thought that probably it would be better to pick out a small committee, with a skilled physicist, because our problem is physical medicine, a skilled lexicographer, and a specialist in the field to work out a set of definitions.

We are confused by such problems as terminology for a procedure such as that in which an electrical constant current is used to introduce the ions of certain drugs into the superficial tissues. For years, physicians have called this procedure "ionization," which is incorrect. Then some purist suggested the term "iontophoresis." That didn't seem satisfactory, and somebody said the term should be "electrophoresis." Now physicists say that we should call this procedure "common ion transfer."

We have the problem of trade names: hypothermy, from a trade device "Hypotherm"; inductothermy, from a trade name "Inductotherm"; endothermy, from a trade name "Endotherm." Shall they be included in a list of definitions or shall they be excluded?

To the uninitiated observer, this conference seems to have been confusing two closely related problems, nomenclature and statistics; terminology, per se, and grouping of terms; if those two could be separated, confusion could be avoided.

Our committee is trying to prepare for clinical purposes an acceptable list of definitions in the field of physical medicine.

#### DISCUSSION

CHAIRMAN EMERSON: Dr. Krusen gave a list of different terms that stem entirely from therapy, and we can no more list therapeutic procedures in this field or drugs than we could in any other special field of application, but so far as your request concerns diagnostic definition we ought to be able to meet your needs.

DR. FRANK H. KRUSEN, Rochester, Minn.: We are not asking that a list of definitions be incorporated into the Standard Nomenclature. We are merely preparing, as part of our Council's work, a revision of a list already published by that Council. We ask only that this he considered by those of the conference who have experience in this particular field of nomenclature. We are interested in nomenclature, not in statistics, as far as this particular committee is concerned. We are merely asking for advice.

### Nomenclature and Classification of Allergic Disorders

DR. SAMUEL M. FEINBERG, Chicago: The difficulties in attempts to delineate and classify disease conditions and scientific terms arise from several sources: 1. The long-continued usage of terms, usually of lay variety, has given an almost indelible stamp to some diseases, even though the appellations create entirely erroneous impressions of the nature of the conditions. 2. The tendency to combine stems from words in Greek and Latin to produce combinations has resulted in hybrid products which are neither scientific nor clear. Anglo-Saxon and Arabic origins also have complicated our etymology. 3. The honor reflected from scientific discoveries has given rise to eponyms, which are neither scientific nor descriptive. 4. Changing concepts of the nature of pathologic conditions result in changing and multiple terms.

I will attempt to throw light on the classification and terminology of the clinical manifestations of allergy. It would be well to define briefly the most important fundamental types of hypersensitiveness. Hypersensitiveness is an increased reactivity to a specific substance which, in normal subjects, produces little or no reaction. Allergy is the usually accepted term for all types of human hypersensitiveness. It may be subdivided into several components. Atopy is a type of hypersensitiveness peculiar to man, subject to hereditary influence, presenting the characteristic specific immediate whealing type of reaction, having the circulating antibody reagin and manifesting certain peculiar clinical syndromes such as asthma and hay fever. Bacterial allergy (tuberculin type) is not subject to hereditary influence, is normally dependent on previous infection to the specific organism, is characterized by the delayed type of infiltrative reaction and does not have any demonstrable circulating antibodies. Contact allergy is a type of hypersensitiveness almost exclusively confined to the epidermis, caused usually by a nonprotein allergen, giving no positive whealing type of reaction but rather a delayed eczematous reaction to prolonged contact with the allergen, and displaying no circulating antibodies. Just because a certain manifestation (asthma, for example) is classed as an allergic disease does not necessarily imply that the inference is made that allergy is the sole cause for every instance of such affliction. The word asthma originates from the Greek, meaning "panting." The majority of authors employ the term "bronchial asthma" to denote the common atopic variety, such as asthma to pollen, foods or animal danders. They differentiate bronchial asthma from asthma due to left ventricular failure (cardiac asthma) and from asthma due to bronchitis. The cardiac asthma is identical in mechanism to the atopic variety,

being spasmodic, presenting the same pathologic and physiologic manifestations in the bronchi and relieved by the same drugs, such as epinephrine. Hence cardiac asthma is bronchial asthma. It is confusing, therefore, to use the term bronchial asthma as it is commonly used. It is proposed that the general term asthma be employed for all such types of spasmodic breathing. If the specific allergic etiologic factor has been located, the condition should be designated allergic asthma.

What shall we name the syndrome of watery rhinorrhea, sneezing and spasmodic blocking? Shall it be hay fever, allergic rhinitis, vasomotor rhinitis, perennial rhinitis, rhinitis vasomotoria, hyperesthetic rhinitis or intumescent rhinitis? Shall we then call this affliction "allergic rhinitis"? Authors of textbooks on allergy have arbitrarily regarded this designation suitable. However, in the present state of knowledge we have no right to assume that other than allergic causes are not instrumental in producing these symptoms. Vasomotor rhinitis is not a good name because it has the same inherent inconsistencies as the term "bronchial asthma." Hyperesthetic rhinitis, we believe, is the most suitable term for this condition, since it describes the essential features of the disease, the sensibility to stimuli. If the nasal symptoms are due to allergic causes then the designation allergic rhinitis is justifiable. Of the latter the most common varieties are the seasonal and the nonseasonal. "Hay fever" has been the most common designation for the seasonal form. This term is a misnomer. The disease is not due to hay nor is it accompanied by fever. It were better to refer to this condition in general as seasonal rhinitis or seasonal allergic rhinitis. If the symptoms are due to pollen, then we may refer to it as pollen rhinitis or pollinosis. The nonseasonal form may be designated as perennial allergic rhinitis.

### CUTANEOUS MANIFESTATIONS

Urticaria is an old established appellation. The origin of the term is derived from the genus of plant Urtica, which has the general property of producing itching swellings on the skin of every one by contact with it. There is no serious objection to this term. Angioneurotic edema is interchangeable often with urticaria and not infrequently the two occur in the same individual in the same attack. Among the definitely known causes of this manifestation is allergy. The objection to the eponymic term Quincke's disease is self evident. The name angioneurotic edema is objectionable because it conveys the impression of a neurosis, which steers away from the truth and tends to deaden the stimulus for future investigation. Probably the most suitable designation would be acute circumscribed edema or perhaps giant urticaria.

Perhaps in no other phase in medical nomenclature is there as much confusion as in the field of "eczema." "Eczema" has been the waste basket of misunderstood, unidentified forms of inflammatory lesions of the skin. In allergy we are concerned principally with two types of so-called eczema. One type is definitely associated with other diseases of atopy, such as asthma and hay fever, in the individual, the family or both. This dermatosis has been called neurodermatitis, generalized neurodermite, neurodermite, flexural eczema, lichen chronicus simplex disseminatus and just eczema. All of these are objectionable on the grounds either that they stamp this dermatosis with a neurogenic character or that the name is not accurately descriptive. There can be no question now of the true atopic nature of this manifestation and since the lesions are truly of the nature of a dermatitis we may as well combine the two ideas and agree with Sulzberger that the most fitting designation for it is atopic dermatitis. The second important variety of allergic dermatitis is one in which the allergy is apparently confined to the epidermis and the inflammation is produced by direct contact. European dermatologists have correctly referred to it for years as "eczema." The name dermatitis is permissible because an eczema is still a dermatitis. However, the contact feature should be expressed in the name, such as contact eczema or contact dermatitis.

For the one-sided familial headache which is so frequently allergic, migraine is an excellent term. Many ophthalmologists believe in the allergic nature of vernal conjunctivitis. There is sufficient evidence to indicate that some of these cases are allergic. The term vernal catarrh, I believe, should be dropped in favor of the former name, since "catarrh" has been another pigeonhole in which an attempt is made to hide our ignorance.

### Classification of Allergic Conditions

DR. J. FREDERICK PAINTON, Buffalo: Like every new conception allergy is being used as an explanation for a great variety of conditions that hitherto has been unexplained. Allergy plays an important role in many diseases but it should not be used as a scapegoat for every obscure disease process. A review of the literature during the past ten years failed to reveal any effort toward the establishment of a basic classification in allergy. In attempting to formulate any sort of recording system of allergy, we must endeavor to establish this classification on both a topographic or regional basis and an etiologic relationship. Every new fiber, every new cosmetic, every new drug is a potential cause of allergy. When we consider the numberless known allergens, it is apparent that there is no advantage in adopting individual allergens as a basis for classification. It might be practical to base this etiology on the mode of production, as by ingestion, inhalation, injection and contact. It also seems necessary to indicate whether the allergy is seasonal or whether it occurs throughout the entire year or perennially. Allergy in the nose is properly called allergic rhinitis. It would be classified under disease of the nose or nasal mucosa. The term hay fever should be abandoned. Allergists feel that the most acceptable name is pollinosis. Thus under the seasonal forms of allergic rhinitis we would place the term pollinosis. To classify pollinosis further as to the exact season is essential because some cases occur in the spring, some in the early summer and some in the fall. The perennial variety is frequently designated as hyperesthetic rhinitis, vasomotor rhinitis or perennial hay fever; obviously the latter term should be avoided. We would classify the condition as allergic rhinitis, perennial, and specify whether it is of the inhalant or ingestant type. If the allergens producing such a condition can be grouped together, such a group as animal emanations, or dust, might be used to specify more definitely if placed in parenthesis.

It might be well to follow the suggestion of Cook and Coca and classify all bronchial asthma as either allergic or nonallergic; if allergic, specify whether perennial or seasonal and then designate in the same fashion in which allergic rhinitis was handled whether it is inhalant, ingestant, injectant or contactant. It might be necessary to add a fifth designation, focal, indicating a sensitivity to bacteria or fungi. As there are other accepted causes of bronchial spasm, we are justified in designating them as nonallergic. In this category would be placed pulmonary fibrosis and pulmonary emphysema with associated bronchial spasm, cardiorenal disease, thymic enlargement and reflex bronchial spasm.

Allergic conditions of the skin constitute an extensive subject but it should be possible to handle it in the same manner as rhinitis and bronchial asthma.

Food allergy, or gastrointestinal allergy, should be placed under disease of the gastrointestinal tract, conforming to the topographic classification. As these cases are practically always the result of food or drugs ingested, they would be obviously called ingestant and better specified in parenthesis food or drugs. However, if this syndrome of gastrointestinal allergy which is usually characterized by nausea and emesis, cramps and diarrhea results from some substance injected naturally, it would be classified as injectant.

Physical allergy, such as hypersensitivity to heat and cold, affects the body as a whole topographically and it would have to be placed in that category. From the standpoint of a mode of production, it would seem logical to consider this type of allergy as contactant.

This classification has its limitations, yet I hope it will serve a useful purpose in the recording of allergic conditions.

### Problems of Dermatologic Nomenclature

DR. HOWARD FOX, New York: The average physician who looks at the list of diseases of the skin in the Standard Nomenclature will think the subject of dermatology is perhaps hopeless. The list includes some diseases which are of mere

academic interest. The last mentioned are, however, important as a background for differential diagnosis.

We have long passed the stage of merely naming diseases of the skin. To listen to some discussions at our national societies, one might think the speakers were physiologists, chemists, pathologists, mycologists or even physicists.

Many of the diseases in our list were named generations ago, before pathogenic organisms were discovered. Some of these names are so universally used that it would be almost impossible to change them. Many of them are fanciful, such as psoriasis, lichen and pemphigus. It would be difficult to change names like these, and it would be unwise until we are certain of their causation.

I realize the trend toward English and away from Latin or Greek words, but I hope that in the next edition of the Classified Nomenclature we may continue to use to a large degree Latin or Greek names for diseases of the skin. One reason for doing so is long usage of these terms. A second reason is consistency. If from 80 to 90 per cent of our terms are in Latin, to be consistent all or nearly all of them should be Latinized. A more important reason is an international one. The only possible international nomenclature is one of Latin or Latinized Greek words. While English is the best modern language for international communication, it is not universally understood.

Certain anatomic terms in Latin or Greek cannot be changed. If we must gradually change our nomenclature to English, at least we should exclude names in French or other modern languages as far as possible. In our dermatologic list we still have one French term, "perlèche," and one Dutch term, "veldt sore." Thus far we haven't been able to get rid of them.

I am in accord with the tendency to omit the name of the person who first described a disease. Our list now contains only three terms which are designated solely by the names of those who first described them. They are Bowen's disease, Fox-Fordyce disease and, of course, Raynaud's disease. We will welcome the deletion of the describers' names when we are able to devise satisfactory titles for the diseases in question. In a few other disorders the name of the describer is mentioned with the disease.

The dermatologists are not the only ones who have plenty of Latin terms. How would the ophthalmologists like to have English substitutes for such terms as amaurosis, amblyopia, arcus senilis, chalazion, ectropion, exophthalmos, iridocyclitis, mydriasis and ptosis? In the revision of the Classified Nomenclature I suggest deletion of the word "infectional," which is used throughout the volume. There is no such word, according to Dorland's, Webster's, the Century, Standard and Oxford dictionaries.

DISCUSSION

DR. MORRIS FISHBEIN, Chicago: A great many of the terms which Dr. Fox characterizes as Latin are now recognized as English, and no one wants to abolish those terms.

## Terminology in Diseases of the Blood-Forming Organs

DR. RAPHAEL ISAACS, Ann Arbor, Mich.: In writing a review of hematology this year, every time I came across a reference in any of the articles appearing in 1939 to "leukemia" or to a lymph gland disease I jotted down the name. There are about sixty-one odd names describing leukemia. There are not that number of types of leukemia. Is this a refined classification? Why are there so many names? I tried to classify these names in some way, and the only classification I could make was to put them in alphabetical order. There seemed to be tremendous overlapping. Which shall we take, "myelogenous leukemia," "myelotic leukemia," "myeloid leukemia"? There seems to be no hope of simplifying this list. It is difficult in hematologic subjects to give a cause of the disease, so we shall have to use some expression which is arbitrary. In this field it would be satisfactory to have in the index all these names with the proper number after them. I think many people would prefer to look in the index under their favorite name and find the classification number right there. It would solve their problems.

Sometimes a stage in a disease is given a name, like "myeloblastic leukemia," which is just a stage probably in the ordinary development of leukemia. Some of the names are clinical, such as "malignant lymphoma"—"lymphoma" because somebody saw a lump in the body where a lymph gland would be, and "malignant" because he couldn't cure it. Some names are pathologic, such as "round cell sarcoma." There is a whole list of names which are the result of looking at a section under the microscope. Are we not to name a disease until we have done a biopsy or until after an autopsy? We must have some name during life. That is one reason for so many names.

Some of these names change so rapidly that it is impossible to keep up with the literature on the subject. Almost every few days an article comes out with a new name of a variation of some old disease. There is often confusion between groups and single diseases or specific diseases. For example, the term "lymphosarcoma" is sometimes used for a whole group of diseases and sometimes for a specific disease. There is confusion with the suffixes. For example "oid" in a term like "myeloid." Is it "myelogenous leukemia" or is it "myelocytic leukemia"? There is the ending "ic," the ending "osis" and the ending "oma," which are all confused.

DISCUSSION

DR. MORRIS FISHBEIN, Chicago: Medicine proceeds by epochs, the epoch of allergy and the epoch of advancement in diseases of the blood. It might be possible in many of these revisions to concentrate on these particular fields which mark an epoch of medical advancement.

## Diseases of Endocrine Origin

DR. ELMER L. SEVRINGHAUS, Madison, Wis.: In line with what Dr. Fishbein has said, the past decade has witnessed the development of definitely identifiable endocrine materials. The same thing might be said for nutritional materials, especially vitamins. We have developed also new tools for measuring function so that we are able to talk in terms of etiology more specifically than ever before.

I might call attention to the type of thing we are advising. On page 84 in the book, the etiologic classification will have to be expanded by the addition of more vitamins. The numbering scheme makes that possible. How long the numbering scheme will be adequate, I do not know. My associate Dr. Gordon says there are now probably something like thirty-one or thirty-two identifiable vitamins. They haven't all had their clinical syndromes described yet.

In the case of the endocrine materials, the number scheme is already sadly taxed, however, because here we must plan for overactivity and underactivity in the case of each gland. There is no hope at this time of trying to assign a different number to disturbances in the growth-promoting glands, the gonadotropic, the thyroidotropic and the anterior pituitary. We shall have to list it simply as anterior pituitary and be satisfied with that. Perhaps that is just as well until we can be certain of chemically identifiable fractions of the pituitary. Even with that in mind we shall have to use every number we can find in the expansion of this scheme, and at the same time we do that we are going to suggest dropping numbers referring to function of the thymus and the pineal until somebody can define functions for those glands.

Another matter is that we should clearly distinguish between growth and development. They are at present listed as one. The number scheme will allow that to be done without much difficulty.

I invite attention to the group called "Diseases of the Psychobiological Unit." There is increasing need in medicine for attention to such a thing as a psychobiologic unit, but there are some reasons for thinking that infantilism and precocity and premature puberty and menopause syndrome don't belong there, since we can begin to assign them to definite etiologic forces or single organs. They are therefore recommended for deletion at that point, since they do appear again in the appropriate place with reference to a given gland.

Similar things can be said about a number of items which appear again, not under psychobiologic units, but under body as a whole. When we get to such things as obesity there is an entire section, from the bottom of page 111 to the middle of page 116. Practically that entire portion of the book we are recommending for deletion, because many of those items appear

later on and some of them will be inserted in other sections at the appropriate place. The places where they will appear will occur at two sites later in the book, one of them in the section which is now devoted to disturbances of the genital system. That is because of the rapid development of genital physiology from an endocrine point of view. Disturbances of the thymus and functional disturbances of the thyroid should all be listed under "thyroid," instead of having "cretinism" listed in one part of the book and "hyperthyroidism" in another part. We believe we can bring together things more logically associated, which can more easily be found, and can have a teaching advantage in showing their association. In general, revision is needed also in the various types of disorders of menstrual function and fertility.

# OFFICIAL NOTES

## THE NEW YORK SESSION

### Change in Date of Session on Anesthesia

It has been found advisable to change the Session on Anesthesia in the Section on Miscellaneous Topics from Wednesday afternoon, June 12, to Thursday afternoon, June 13. This will enable all those interested to attend the Session on Anesthesia on Thursday afternoon and the Symposium on Anoxia in the Section on Pathology and Physiology on Wednesday afternoon if they so desire.

### Registration

The Bureau of Registration will be located on the second floor of the Grand Central Palace, Lexington Avenue between Forty-Sixth and Forty-Seventh streets. Fellows are urged to bring with them their 1940 Fellowship Cards, which will facilitate registration. Any Fellows who have not received cards for 1940 should secure them at once by writing to the American Medical Association, 535 North Dearborn Street, Chicago, Ill.

# MEDICAL LEGISLATION

## MEDICAL BILLS IN CONGRESS

*Changes in Status.*—The House Committee on Mines and Mining has held a hearing on S. 2420, already passed by the Senate, proposing to authorize the Secretary of the Interior to make certain inspections and investigations in coal mines for the purpose of obtaining information relating to health and safey conditions, accidents and occupational diseases therein. S. J. Res. 256, introduced by Senator Bilbo, Mississippi, has been reported favorably to the Senate by the Committee on the Library, proposing to designate a day to be observed as Doctor's Day.

*Bills Introduced.*—H. Res. 493, introduced by Representative Rankin, Mississippi, proposes to authorize the House Committee on World War Veterans' Legislation or any subcommittee thereof to make a comprehensive survey and inspection of soldiers' hospitals and other Veterans' Administration facilities, including any hospital with which the government has a contract for ex-service men of any war in which the United States was engaged. The committee is to be authorized to make a report of its findings to the House, accompanied by such recommendations in the form of a bill or otherwise as it may deem necessary. H. R. 9735, introduced by Representative Ramspeck, Georgia, is a bill "To encourage and promote the highest standards of service among officers and employees of the United States by creating the Association of Government Employees." Among other things, this corporation is to be authorized to engage in educational, charitable, recreational, athletic, social, health, mutual benefits and cooperative activities, and to maintain and operate facilities incidental thereto. H. R. 9777, introduced by Representative Voorhis, California, proposes to promote national health and welfare through appropriations for hospitals and for prevention, education and control of tuberculosis. S. 3924, introduced by Senator Wagner and referred to briefly in THE JOURNAL last week, proposes to amend the Social Security Act so as to provide insurance benefits for wage earners permanently and totally disabled for causes not arising out of their employment. In addition to cash benefits to be paid, the bill proposes that the Social Security Board may make provisions for the furnishing of medical, surgical, institutional, rehabilitation or other services to individuals entitled to such cash benefits, if such services may aid in enabling such individuals to return to gainful work. The bill provides that such services shall be furnished by qualified "practitioners" and through governmental and nongovernmental hospitals and other institutions qualified to furnish such services.

# WOMAN'S AUXILIARY

### Illinois

At a meeting of the auxiliary to the Adams County Medical Society in Quincy, Dr. Arthur Bitter spoke on "Advances in Surgical Treatment and Operations."

Members held a round table discussion on socialized medicine at the meeting of the auxiliary to the Sangamon County Medical Society in Springfield December 11.

Dr. Melvin F. Blaurock, psychiatrist at the Institute of Juvenile Research, gave an illustrated lecture on "A New Approach of the Problems of Juvenile Delinquency" at a meeting of the auxiliary to the Will-Grundy County Medical Society in Joliet.

### Oregon

The auxiliary to the Benton County Medical Society is collecting books for a library for the patients in Corvallis General Hospital.

The auxiliary to the Clatsop County Medical Society has done much sewing for patients in the Doernbecher Memorial Hospital for Children in Portland.

The auxiliary to the Coos and Curry County Medical Society met in North Bend January 16. The main project of the auxiliary is helping the needy at the county farm in Coquille.

The auxiliary to the Harney County Medical Society has 100 per cent membership. *Hygeia* has been placed in all schools in the county by the auxiliary's cooperation with the Harney County Health Association.

### Washington

The auxiliary to the King County Medical Society held meetings in Seattle in November, December and January. Dr. Edwin Guthrie discussed "Human Relationships"; Dr. and Mrs. Austin DeFreece, European travel; Mrs. L. S. Roach, the philanthropic fund of the auxiliary, and Senator Pearl Wanamaker, the "Human Side of the Legislature."

The auxiliary to the Pierce County Medical Society was host to the auxiliary to the Washington State Medical Association at its midyear board meeting in Tacoma February 16.

The annual guest day of the auxiliary to the Spokane County Medical Society was held on January 12. A panel discussion was presented as follows: Dr. M. S. Wright, public health; Dr. C. L. Lyon, pediatrics; Drs. J. B. Plastino and T. I. Moore, socialized medicine; Mrs. I. Hanks, Spokane County Public Health Council. Dr. Moore also spoke on the platform of the American Medical Association and the Wagner Health Bill. More than 125 persons attended the meeting.

# Medical News

(Physicians will confer a favor by sending for this department items of news of more or less general interest: such as relate to society activities, new hospitals, education and public health.)

Additional medical college news and articles appear in the Student Section, page 2157.

## ALABAMA

**Personal.**—The Houston County Medical Society gave a dinner recently in honor of Dr. Mercer S. Davie, Dothan, then president of the Medical Association of the State of Alabama, and presented him with a traveling case and fitted week-end bag. Dr. Marye Y. Dabney, Birmingham, as guest speaker, discussed "The Use of Hormones in Gynecology."

**Society News.**—Dr. Merle E. Smith, Parrish, addressed the Walker County Medical Society, Jasper, April 12, on "Pregnancy and Cervical Carcinoma."——The Calhoun County Medical Society was addressed in Anniston recently by Dr. James S. McLester, Birmingham, on "Diet in Heart Disease" and Dr. David H. Poer, Atlanta, "The Diagnosis and Treatment of Thyroid Conditions in the Southern Area."

**Postgraduate Lectures.**—A series of postgraduate lectures in internal medicine opened in Montgomery, April 26, to continue for six weeks, for the benefit of physicians in Montgomery, Bullock, Autauga, Elmore and Lowndes counties. The lecturers are Drs. William A. Sodeman and Julius L. Wilson, instructor in medicine and associate professor of medicine, respectively, Tulane University of Louisiana School of Medicine, New Orleans. It is also planned to give the same lectures in Dothan, Troy, Eufaula and Greenville.

## CONNECTICUT

**Dr. Francis Blake Made Acting Dean of Yale.**—Dr. Francis G. Blake, Sterling professor of medicine, Yale University School of Medicine, New Haven, has been appointed acting dean of the school. Dr. Stanhope Bayne-Jones is retiring as dean July 1. Dr. Blake graduated at Harvard Medical School in 1913. He was a member of the staff of Peter Bent Brigham Hospital from then until 1916, when he went to the Rockefeller Institute for Medical Research for a year. From 1917 to 1919 he was associate professor of medicine at the University of Minnesota Medical School, Minneapolis. The following year he was associate in medicine at Rockefeller Hospital and from 1920 to 1921 associate member of the Rockefeller Institute; he was a member of its scientific board of directors from 1924 to 1935. He joined the Yale faculty as John Slade Ely professor of medicine in 1921 and served until 1927, when he was made Sterling professor of medicine. Among other positions Dr. Blake has been chairman of the division of medical sciences, National Research Council, 1933-1936; chairman of the Section on the Practice of Medicine, American Medical Association, 1938, and president of the American Society for Clinical Investigation and American Association of Immunologists.

## GEORGIA

**Personal.**—Dr. Stuart P. Vandiviere has resigned as health commissioner of Americus-Sumter County to accept an assignment for duty with the U. S. Army air corps at Maxwell Field, Ala., newspapers reported. Dr. Henry T. Adkins, Cochran, has been appointed to succeed Dr. Vandiviere.

**Society News.**—Dr. Albert Worth Hobby presented a paper before the Fulton County Medical Society, Atlanta, April 4, entitled "Air Embolism Following Pneumothorax." Dr. Frank Lee Bivings presented a paper before the society, April 18, entitled "Relation of Asthmatic Bronchitis to Chronic Upper Respiratory Infections in Children: A Five Year Study of 235 Cases."

**State Medical Election.**—Dr. Allen H. Bunce, Atlanta, was chosen president-elect of the Medical Association of Georgia at its annual session in Savannah in April and Dr. Job C. Patterson, Cuthbert, was installed as president. Other officers are Drs. Julian K. Quattlebaum, Savannah, and Marion T. Benson Jr., Atlanta, vice presidents, and Dr. Edgar D. Shanks, Atlanta, secretary-treasurer. Dr. Bunce once held the office of secretary-treasurer for fifteen years. In 1941 the association will meet in Macon, May 13-16.

## ILLINOIS

**Society News.**—Dr. Friedrich P. E. Bornstein, Rochester, among others, addressed the Sangamon County Medical Society in Springfield, May 2, on "Pharmacology of the Myocardium." Dr. Ralph H. Major, Kansas City, Mo., addressed the society, April 4, on "Therapy of Endocarditis Lenta."——Dr. Lee C. Gatewood, Chicago, discussed "Dysentery Including Amebic Dysentery" before the Madison County Medical Society in Highland, May 3.——Dr. James H. Hutton, Chicago, discussed "Recent Development in Endocrine Diagnosis and Therapy" before the Adams County Medical Society in Quincy, April 8.

### Chicago

**Alumni Day at University of Chicago.**—Alumni of the Division of Biological Sciences, University of Chicago, will hold their annual assembly June 7. The speakers at the scientific sessions will include:

Dr. Charles B. Huggins, The Prostate Problem.
Dr. Lester R. Dragstedt, Recent Work with Lipocaic.
Dr. Dwight F. Clark, Treatment of Psoriasis with Lipocaic.
Dr. Keith S. Grimson, Surgical Treatment of Hypertension.
Dr. Henry T. Ricketts, Constancy of Action of Protamine Zinc Insulin.
Dr. Walter E. Hook, Studies on Hibernation.
Dr. Carl C. Pfeiffer, The Therapy of Migraine Headaches.
Dr. Curtis M. Flory, Production of Tumors by Tobacco Tars.
Dr. Francis B. Gordon, Inapparent Virus Infections in the White Rat.
Dr. Paul E. Ross, Some Impressions of Ovarian Neoplasms in Slye Mice.
Dr. Jonathan M. Williams, Cleveland, Use of Erythroidine in Metrazol Therapy.
Dr. Abraham Kauvar, Boeck's Sarcoid (Schaumann's Disease).
Dr. V. Brown Scott, Bloomington, Ind., Observations on the External Pancreatic Secretions in the Fasting Dog.

**Alumni Reunion.**—Alumni of Rush Medical College will hold a reunion at the college June 6-7. The program includes symposiums on endocrines, chemotherapy, abdominal surgery, gastro-enterology, cardiovascular renal disease and traumatic surgery, and the following speakers, among others:

Dr. James W. Merricks, What About the Irritable Bladder in Women?
Dr. George E. Shambaugh Jr., Operative Restoration of Hearing in Otosclerosis.
Drs. Carl W. Apfelbach and Ernest E. Irons, Aspiration Bronchopneumonia.
Dr. John H. Olwin, Methods for Estimation of Prothrombin Levels and Administration of Vitamin K.
Dr. Evans W. Pernokis, Adequate Control of Pernicious Anemia.
Dr. Paul A. Campbell, Profound Physiologic Effects of Modern High-Speed, High-Altitude Military Flying.
Dr. Herman L. Kretschmer, Significance of Blood in the Urine.
Dr. Archibald L. Hoyne, Old and New Methods in the Treatment of Meningitis.
Dr. Herbert C. Breukaus, The Neutralizing Capacity of Antacids.
Dr. Hillier L. Baker, Acromial and Subacromial Bursitis: Treatment by Local Infiltration and Excision.
Dr. Aaron Arkin, Primary Carcinoma of the Lung—A Prevalent Disease.
Dr. Heyworth N. Sanford, Thromboplastic Factors in Coagulation.
Dr. Clayton J. Lundy, Early Diagnosis of Coronary Sclerosis.
Dr. Clark W. Finnerud, Skin Cancer.
Dr. Adrien H. P. E. Verbrugghen, Head Injuries.

The annual banquet at the Stevens Hotel, Thursday evening, will be addressed by Dr. Morris Fishbein, Editor of The Journal. At 7 o'clock, Friday evening, a reunion of Presbyterian Hospital interns will take place in the Oceanic Room of the Knickerbocker Hotel.

## INDIANA

**Society News.**—The Indianapolis Medical Society will be addressed, May 28, by Drs. Edwin L. Libbert, Lawrenceburg, on "Medical Application of Physical Medicine," and Edwin N. Kime, "Surgical Application of Physical Medicine." The society was addressed, May 14, by Dr. Percy S. Pelouze, Philadelphia, on gonorrhea.

**Changes in Health Officers.**—Dr. Walter M. McGaughey, Greencastle, has been appointed health officer of Putnam County to fill the unexpired term of Dr. William M. O'Brien, resigned. The latter's term was to have ended Dec. 31, 1941.——Dr. Claude D. Greene, Spencer, was recently named health officer of Owen County, succeeding Dr. Boaz Yocum, Coal City, who held the position for ten years.——Dr. Paul P. Bailey, Fort Wayne, has been appointed health officer of Allen County, succeeding Dr. Noah A. Rockey.

## MASSACHUSETTS

**Dr. Parran Lectures on the Nation's Health.**—Dr. Thomas Parran, surgeon general, U. S. Public Health Service, Washington, D. C., gave the fourteenth William Thompson Sedgwick Memorial Lecture of the Massachusetts Institute of Technology, Cambridge, April 11. His subject was "Nutrition and the Nation's Health."

**Society News.**—The Boston Gastroenterological Society was addressed, April 3, by Drs. Charles W. Finnerty on "The Treatment of Peptic Ulcer Complicated by Diabetes Mellitus"; Timothy F. P. Lyons and Marino F. Vidoli, "Rectal Polyps: A Pathologic Discussion," and Louis F. Curran, "Achlorhydria."—Dr. Arthur M. Fishberg, New York, discussed "Essential Hypertension" before the Greater Boston Medical Society, April 2.—Dr. Moses Ralph Kaufman, Boston, addressed the New England Society of Psychiatry in Hathorne, April 24, on "Factors in Psychotherapy: A Psychoanalytic Evaluation."—Dr. Hamilton Montgomery, Rochester, Minn., discussed "Pathologic Features of Some of the Non-Neoplastic Dermatoses" before the New England Pathological Society in Boston, April 18.

## MICHIGAN

**Personal.**—Dr. Charles E. Stewart, director of the Battle Creek Sanitarium, Battle Creek, has announced that he will retire at the end of the year, newspapers reported. Until then Dr. Stewart will serve as adviser to Dr. John E. Gorrell, who was appointed administrator at the sanatorium in October 1939. Dr. Stewart joined the staff of the sanitarium in 1895; in 1917 he was made associate director and subsequently director.—Paul H. Jeserich, D.D.S., Ann Arbor, has been appointed a member of the state council of health for the term ending June 30, 1945, succeeding Dr. Carleton Dean, Charlevoix, who resigned recently to become deputy state health commissioner. Dr. Jeserich is president of the Michigan State Dental Society and director of postgraduate education at the University of Michigan School of Dentistry.

## MINNESOTA

**State Medical Election.**—Dr. Berton J. Branton, Willmar, was chosen president-elect of the Minnesota State Medical Association at its annual meeting in Rochester in April and Dr. Bertram S. Adams, Hibbing, was installed as president. Drs. Albert Fritsche, New Ulm, and Frank J. Heck, Rochester, were elected vice presidents. The 1941 meeting will be in St. Paul. Dr. Carl W. Waldron, Minneapolis, was awarded the prize presented each year by the Southern Minnesota Medical Association for the best scientific exhibit at the state meeting. His theme was "Fractures of the Facial Bones."

## MISSISSIPPI

**Hospital News.**—The Beacham Memorial Hospital was recently opened in Magnolia by Drs. Aubrey V. Beacham, Magnolia, Hugh T. and Woodard D. Beacham, New Orleans, all brothers, as a memorial to their father. Dr. George W. Robertson, Magnolia, made the principal address. Dr. Rudolph Matas, New Orleans, also spoke at the dedicatory ceremony.

## MISSOURI

**Personal.**—Dr. Mary Jeanette Lower, Kansas City, was presented with the Award of Honor of the Soroptimist Club of Kansas City at a banquet in her honor, May 6. Dr. Lower is a charter member of the club, which is one of 175 similar organizations that make up the American Federation of Soroptimist Clubs of Professional and Executive Business Women. Membership is by invitation only and only one member of each classification is eligible.

**Annual Clinic.**—The St. Joseph Clinical Society held its ninth annual two day spring clinic at the Hotel Robidoux, St. Joseph, recently. The following participated:

Dr. Robert Elman, St. Louis, Intravenous Fluids in the Surgical Patient with Special Reference to Protein Replacement.
Dr. Emil D. W. Hauser, Chicago, Low Back Pain Due to Functional Decompensation.
Dr. Lee Forrest Hill, Des Moines, Iowa, Changes Produced by Severe Diarrhea and Their Restitution.
Dr. Virgil E. Simpson, Louisville, Ky., Criteria for Classification and Diagnosis of Heart Disease.
Dr. Leo G. Rigler, Minneapolis, Roentgen Diagnosis of Acute Abdominal Conditions and Bronchial Asthma.
Dr. William B. Kountz, St. Louis, The Heart and Vascular System in Middle Age and Its Importance in Clinical Medicine.
Dr. Paul A. O'Leary, Rochester, Minn., The Eczemas.
Dr. Joseph C. Birdsall, Philadelphia, Incidence of Urinary Tract Obstruction in Renal Disease.
Dr. Lester D. Powell, Des Moines, Consideration and Surgical Treatment of Uterine Prolapse.
Dr. Lathan A. Crandall Jr., Memphis, Tenn., Vitamin B and Functional Digestive Disturbances.

At a banquet the speakers were Dr. Simpson on "Chemotherapy of Pneumonia"; Dr. Charles W. Mayo, Rochester, "Malignancy of the Right Colon," and Dr. O'Leary, "The Treatment of Syphilis." Dr. Paul C. Barton, Director, Bureau of Investigation, American Medical Association, Chicago, addressed a preconvention evening meeting on "'Patent Medicines'—Old and New."

## NEW JERSEY

**State Medical Meeting at Atlantic City.**—The one hundred and seventy-fourth annual meeting of the Medical Society of New Jersey will be held at Haddon Hall, Atlantic City, June 3-6, under the presidency of Dr. Edward Zeh Hawkes, Newark. Among the speakers will be:

Dr. Hobart A. Reimann, Philadelphia, Functional Gastrointestinal Disorders.
Dr. Fritz H. Lewy, Philadelphia, Neurologic Manifestations of Nutritional Deficiencies.
Dr. Martin G. Vorhaus, New York, A Clinical Survey of the Vitamin B Complex and Its Components.
Dr. George P. Müller, Philadelphia, Complications of Peptic Ulcers: Diagnosis and Treatment.
Dr. Lewis C. Scheffey, Philadelphia, Problems Encountered in the Diagnosis and Treatment of Uterine Cancer.
Dr. Charles C. Higgins, Cleveland, Implantation of Ureters.
Dr. Thomas Fitz-Hugh Jr., Philadelphia, Gastrointestinal Disturbances in the Hemorrhagic Blood Dyscrasias.
Dr. William D. Stroud, Philadelphia, Gastrointestinal Disturbances in Cardiovascular Diseases.
Dr. Frank H. Lahey, Boston, Surgery of the Biliary Ducts and Their Complications.
Drs. Chevalier L. Jackson, William A. Swalm and Lester M. Morrison, Philadelphia, Gastritis, Diagnosis and Treatment.
Drs. Marion B. Sulzberger and Rudolf L. Baer, New York, Dermatologic Manifestations of Gastrointestinal Disease and Nutritional Deficiencies.
Dr. Samuel Bellet, Philadelphia, Effect of Tobacco Smoke and Nicotine on the Normal Heart and in the Presence of Myocardial Disease Produced by Coronary Artery Ligation: An Experimental Study in Dogs.
Dr. Sydney R. Miller, Baltimore, Chronic Nephritis and Its Treatment in the Light of Contemporary Renal Physiology.
Dr. Emil Novak, Baltimore, Endocrine Aspects of Primary Dysmenorrhea.
Dr. Leonard G. Rowntree, Philadelphia, Hypertensulinism.
Dr. Edward L. Bauer, Philadelphia, Rheumatic Infections in Children.
Dr. Thomas A. Shallow, Philadelphia, Surgical Treatment of Gastric and Duodenal Ulcer.
Dr. Henry W. Cave, New York, Cancer of the Rectum.
Dr. Douglas P. Murphy, Philadelphia, Studies in Uterine Motility.

Arthur T. Vanderbilt, LL.D., Newark, professor of law, New York University Law School, will address a general session on "What Is Needed Now." The thirteenth annual meeting of the Woman's Auxiliary to the Medical Society of New Jersey will be at Haddon Hall, June 4-6.

## NEW YORK

**State Medical Election.**—Dr. James M. Flynn, Rochester, was elected president of the Medical Society of the State of New York at the annual meeting in New York, May 7, and Dr. Samuel J. Kopetzky, New York, was chosen president-elect. It was necessary to elect a president because of the death of Dr. James H. Borrell, Buffalo, chosen president-elect at the 1939 meeting. Dr. Albert A. Gartner, Buffalo, was elected vice president and Dr. Peter Irving, New York, was reelected secretary. Next year's meeting will be in Buffalo.

**Professor of Anatomy Appointed at Rochester.**—Karl E. Mason, Ph.D., associate professor of anatomy at Vanderbilt University School of Medicine, Nashville, has been appointed professor and head of the department of anatomy at the University of Rochester School of Medicine and Dentistry, Rochester, N. Y., according to *Science*. He will succeed Dr. George W. Corner, who recently was appointed director of the department of embryology of the Carnegie Institution. Dr. Mason is a Canadian and took his doctor's degree at Yale University, New Haven, Conn., in 1925. He went to Vanderbilt in 1927 as instructor in anatomy; he became assistant professor in 1929 and associate professor in 1930.

### New York City

**Society News.**—The program of the stated meeting of the New York Academy of Medicine, May 2, was devoted to "Problems of Aging." The speakers were Drs. George Morris Piersol, Philadelphia, on the general problem; Ernst P. Boas, cardiovascular problems, and Foster Kennedy, neuropsychiatric problems.—At a meeting of the New York Neurological Society with the section of neurology and psychiatry of the New York Academy of Medicine, May 7, the speakers were Drs. Hiram H. Merritt, Boston, and Tracy J. Putnam, on "Periodic Dulness as an Epileptic Equivalent"; Herbert Jasper, D.Sc., Montreal, Canada, "Electro-Encephalographic Localization of Focal Cerebral Lesions," and Dr. Lawrence S. Kubie, "The Repetitive Core of Neurosis."

**Personal.**—The staff of Morrisania Hospital gave a dinner, May 4, in honor of five members of its staff: Drs. Nathan B. Van Etten, President-Elect of the American Medical Association; Terry M. Townsend, immediate past president of the Medical Society of the State of New York; George E. Milani, president of the Bronx County Medical Society; Harry Aranow, member of the council of the state society, and William

L. Bollens, D.D.S., president of the Bronx County Dental Society.——Dr. Herbert S. Gasser, director of the Rockefeller Institute for Medical Research, has been chosen to receive the honorary degree of doctor of science from the University of Wisconsin at the June commencement.

## OHIO

**Personal.**—Dr. Neal D. Carter, Columbus, has been appointed head of the adult hygiene division of the state health department, it is reported.——Dr. William M. Skipp, Youngstown, who was to be installed as president of the Ohio State Medical Association at the annual meeting in Cincinnati, May 14-16, was honored by the Mahoning County Medical Society with a dinner at the Youngstown Club, May 8.——Dr. Ralph B. Taylor, Columbus, has been appointed a member of the state medical board to succeed Dr. Louis T. Franklin, Chillicothe.——Dr. Arlington J. Rawers, Mendon, has been appointed health officer of Mercer County to succeed the late Dr. Frank E. Ayers, Celina.

**Society News.**—Dr. Waltman Walters, Rochester, Minn., addressed the Academy of Medicine of Cleveland, April 19, on "Surgical Treatment of Lesions of the Gallbladder and Bile Ducts."——Dr. Milton B. Cohen, Cleveland, addressed the Mahoning County Medical Society, Youngstown, March 19, on "The Clinical Problems in Allergy."——Dr. George T. Pack, New York, addressed the Guernsey County Medical Society, Cambridge, recently, on "Cancer of the Stomach."——Dr. John Henry Lazzari, Cleveland, addressed the Lorain County Medical Society, Lorain, recently on "Cancer Management and Therapy."——Dr. Frank W. Anzinger addressed the Clark County Medical Society, Springfield, recently on "Diabetes Mellitus: Etiology, Diagnosis, Treatment and Prevention of Complications."——Dr. Roger O. Egeberg, Cleveland, discussed "Treatment of Asthma" before the Portage County Medical Society, Kent, recently.——Dr. Elmer L. Sevringhaus, Madison, Wis., addressed the Columbus Academy of Medicine recently on "Endocrine Therapy in General Practice."

## PENNSYLVANIA

**Wilkes-Barre Postgraduate Conference.**—Mercy Hospital, Wilkes-Barre, presented its seventh annual postgraduate conference, April 25, with the following speakers:

Dr. Belford C. Blaine, Pottsville, The Program of the Commission on Diabetes of the State Medical Society.
Dr. Joseph T. Beardwood Jr., Philadelphia, Diabetes as a Complication of Other Diseases.
Leon C. Chesley, Ph.D., Jersey City, N. J., Biochemistry of the Toxemias of Pregnancy.
Dr. M. Herbert Barker, Chicago, The Ionic Control of Edema.
Dr. John Scudder, New York, Shock: Blood Studies as a Guide to Therapy.

### Philadelphia

**Schmookler Lecture.**—Dr. Marion B. Sulzberger, New York, delivered the Henry B. Schmookler Memorial Lecture at Mount Sinai Hospital, May 6, on "Some Present Concepts of Dermatologic Allergy, with Particular Reference to Their Application in Practice."

**Society News.**—The orthopedic section of the Philadelphia County Medical Society and the Baltimore Orthopedic Society held a joint meeting at Jefferson Medical College recently. The speakers were Drs. Charles C. Chapple, Philadelphia, on "Congenital Deformities in Children"; Morris Thomas Horwitz, Philadelphia, "Investigation of the Surgical Anatomy of the Knee Joint"; Benjamin Franklin Buzby, Camden, N. J., "End Results of Excision of the Elbow," and Edwin O. Geckeler, Philadelphia, "An Accurate Method of Subcutaneous Internal Fixation for Fracture of the Hip." The commentators, all of Baltimore, were Drs. I. William Nachlas, Allen F. Voshell, Harold R. Bohlman and George E. Bennett.——Dr. Howard B. Sprague, Boston, addressed the Philadelphia Heart Association at its annual meeting, April 10, on "Treatment of Congestive Failure During Active Rheumatic Infection" and Dr. Thomas M. McMillan reviewed the association's work during the past year.——Dr. Frank L. Apperly, Richmond, Va., delivered the annual conversational lecture of the Pathological Society of Philadelphia, April 11, on "The Chemical Function of the Stomach in Health and Disease."

## TEXAS

**Society News.**—At a meeting of the Hunt-Rockwall-Rains Counties Medical Society in Greenville, April 9, the speakers were Drs. Lawrence W. Johnston, Terrell, on "Carbuncle of the Kidney"; Samuel D. Whitten, Greenville, "Superficial X-Ray" and William M. Dickens, Greenville, "General Considerations of the Use of Radiation Therapy with Reference to Some Specific Diseases."——Dr. Idys Mims Gage, New Orleans, addressed the Jefferson County Medical Society, Beaumont, in March, on "Abdominal Complications of Acute Appendicitis."——Speakers before the Dallas County Medical Society, April 25, included Drs. Arthur J. Schwenkenberg, Dallas, on "Metrazol and Insulin Treatment in Psychiatry" and Milford O. Rouse and Cecil O. Patterson, "Foreign Bodies of the Stomach Observed Through the Gastroscope."

## WISCONSIN

**Surgical Meeting.**—The Milwaukee Society of Clinical Surgery held a joint meeting with the Wisconsin chapter of the International College of Surgeons, recently. Operative clinics were conducted at the Milwaukee County Hospital and in the afternoon and evening the following papers were presented:

Dr. Rudolph W. Roethke, Milwaukee, Cervical Pregnancy.
Dr. Frank D. Dickson, Kansas City, Mo., Foot Imbalance.
Dr. Karl Schlaepfer, Milwaukee, Plastic Epiplotis.
Dr. William J. Carson, Milwaukee, Lymphosarcoma of the Ileum.
Dr. Frederick M. Douglass, Toledo, Ohio, Further Studies of End Results in Common Duct Obstruction.

## GENERAL

**Vitamin Research Prize Awarded.**—A prize of $1,000 offered by Mead Johnson and Company for advances in knowledge of the vitamin B complex was awarded at the annual meeting of the American Institute of Nutrition in New Orleans, March 13, for two achievements in investigation. The recipients were Dr. William H. Sebrell Jr., National Institute of Health, Washington, D. C., for the discovery of riboflavin and its use in keratitis; and a group from the research laboratories of Merck and Company, Rahway, N. J., for synthesis of vitamin $B_6$, now known as pyridoxine, John C. Keresztesy, Ph.D., Joseph R. Stevens, Ph.D., Stanton A. Harris, Ph.D., Eric T. Stiller, Ph.D., and Karl A. Folkers, Ph.D.

**Parking Facilities for Physicians.**—An "at the door" parking service will be available at the Grand Central Palace by the "20th Century Garage, Inc.," during the annual session of the American Medical Association in New York, June 10-14. This service has been created in order to relieve the parking problem of patrons and facilitates entrance to the Palace by car. Patrons drive to the main entrance where uniformed attendants deliver a claim check for cars and drive them to the garage. On departing the patron merely presents the claim check to the doorman, who telephones the garage and an attendant then delivers the car to the entrance of the Palace. The rates are as follows:

Two hours 50 cents, 10 cents each hour thereafter; $1 all day, $1.50 for twenty-four hours. Special daily and weekly rates for exhibitors. Pick up and delivery charge included.

**Association for Thoracic Surgery.**—The annual meeting of the American Association for Thoracic Surgery will be held at the Hotel Statler, Cleveland, June 6-8. Included among the speakers will be:

Drs. Adrian V. S. Lambert, Edward P. Eglee and Robert H. Wylie Jr., New York, Empyema and Unexpanded Lung Problems in Pneumothorax.
Dr. David T. Smith, Durham, N. C., Treatment of Fungous Infections of the Lung.
Dr. Leo Eloesser, San Francisco, Further Experiences with Blocked Cavities in Pulmonary Tuberculosis.
Drs. Jacob J. Singer, John C. Jones, and Leon J. Tragerman, Los Angeles, Aseptic Pleural Adhesions Experimentally Produced.
Drs. Chevalier L. Jackson and Archibald R. Judd, Philadelphia, The Role of Bronchoscopy in the Treatment of Pulmonary Abscess.
Drs. Burr Noland Carter, Jean M. Stevenson and Osler A. Abbott, Cincinnati, Esophago-Gastrostomy—An Experimental Study.

There will also be a symposium on bronchospirography by Drs. George C. Leiner and Max Pinner, New York, and William A. Zavod, Mount Vernon, N. Y.; David Salkin, Hopemont, W. Va., and Carl G. Merkel, Mount Morris, N. Y.

**Academy of Tuberculosis Physicians.**—The American Academy of Tuberculosis Physicians will hold its fifth annual meeting at the Commodore Hotel, New York, June 10-11, under the presidency of Dr. Benjamin P. Potter, Jersey City. The speakers will include:

Dr. Felix Baum, Newark, N. J., Rare Cases of Bilateral Idiopathic Spontaneous Pneumothorax in Nontuberculous Individuals.
Dr. Robert B. Mitchell Jr., Baltimore, Eventration of the Diaphragm with Symptoms Resembling Cardiac Disease.
Dr. Hugh G. Whitehead Jr., Baltimore, Sarcoids: Manifestations of Tuberculosis Without Allergy, with Studies on the Possible Etiological Relationship of Acid-Fast Chromogen.
Dr. Jacob W. Cutler, Philadelphia, The Scientific Determination of Erythrocyte Sedimentation Rate.
Dr. William F. Rienhoff Jr., Baltimore, Bronchiogenic Carcinoma.

Dr. George G. Finney, Baltimore, Lung Abscess.
Dr. James L. Dubrow, Des Moines, Iowa, Primary Bronchiogenic Carcinoma.
Dr. Ephraim T. Lisansky, Baltimore, A Method of Case-Finding for General Use.

**Meeting of Ophthalmologists.**—The American Ophthalmological Society will hold its seventy-sixth annual meeting at The Homestead, Hot Springs, Va., June 3-5. The speakers will include:

Dr. Martin Hayward Post, St. Louis, Sterilization of Sharp Instruments by Chemical Solutions.
Dr. Derrick T. Vail Jr., Cincinnati, Anterior Scleral Staphyloma and Retinal Detachment Cured by Excision.
Dr. Charles M. Swab, Omaha, Death Following Operation for Cataract: Report of Three Cases.
Dr. Phillips Thygeson, New York, Sulfanilamide Therapy of Inclusion Conjunctivitis.
Dr. Trygve Gundersen, Boston, Convalescent Blood for Herpes Zoster.
Dr. Frederick H. Verhoeff, Boston, A Case of Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis) Without Glandular Involvement.
Drs. Harold G. Scheie and Francis Heed Adler, Philadelphia, The Site of the Disturbance of Tonic Pupils (Adie's Syndrome).
Drs. Peter C. Kronfeld, Chicago, C. K. Liu, and T. H. Luo, Peiping, China, The Protein Content of the Re-Formed Aqueous Humor in Man.

**Red Cross Appeals for Funds.**—The American Red Cross has issued a nationwide appeal for funds for a minimum war relief fund of $10,000,000 to continue and expand essential activities on behalf of civilian victims of the hostilities in Europe. According to an announcement, the Red Cross had, May 6, spent close to $1,500,000, most of it from reserve funds. More than $300,000 additional had been spent by chapters in purchasing materials for production of relief supplies. Up to May 6 the 250,000 volunteer Red Cross workers had given more than 3,000,000 hours of their time since last September in the production of 447,000 warm garments and 2,261,000 surgical dressings. These supplies, along with tons of drugs and medicines, surgical instruments, x-ray equipment, ambulances, hospital tents, soap and other material have been shipped periodically to the Red Cross societies of war-affected countries. Aid is now being provided to Belgium, Luxembourg, the Netherlands, Finland, France, Norway, England, German-occupied Poland, Latvia, Lithuania, Rumania, Hungary and Yugoslavia. The announcement stated that the Red Cross societies of all countries involved in armed conflict in Europe have requested aid except Germany.

**Special Society Elections.**—Thorne M. Carpenter, Ph.D., Nutrition Laboratory, Carnegie Institution, Boston, was elected president of the American Institute of Nutrition at the annual meeting in New Orleans, March 13; Albert G. Hogan, Ph.D., Columbia, Mo., vice president, and Leonard A. Maynard, Ph.D., Ithaca, N. Y., secretary.——Dr. Stanhope Bayne-Jones, New Haven, Conn., was elected president of the American Association of Pathologists and Bacteriologists at the annual meeting in Pittsburgh, March 20. Dr. Samuel R. Haythorn, Pittsburgh, was chosen vice president and Dr. Howard T. Karsner, Cleveland, reelected secretary.——Dr. John de J. Pemberton, Rochester, Minn., was chosen president-elect of the American Association for the Study of Goiter at the annual meeting in Rochester, April 15. Dr. Frank E. Rogers, Denver, became president. Boston was tentatively named as the place of the 1941 meeting.——Dr. Louis Hamman, Baltimore, was elected president of the Association of American Physicians at its annual meeting in Atlantic City, May 8. Other officers include Drs. James H. Means, Boston, vice president; Hugh J. Morgan, Nashville, Tenn., secretary, and William S. McCann, Rochester, N. Y., treasurer.

**Reunions in New York.**—The committee on university dinners announces that the following organizations have made definite arrangements for reunions during the annual session of the American Medical Association in New York:

Johns Hopkins University School of Medicine, Baltimore, dinner June 12.
New York Post-Graduate Medical School and Hospital, luncheon, June 12.
Harvard Medical School, Boston, dinner, June 12.
Columbia University College of Physicians and Surgeons, New York, dinner, June 12; luncheon, June 13.
Northwestern University Medical School, Chicago, dinner, June 12.
Phi Beta Pi and Alpha Upsilon Omega, joint luncheon, June 12.
Alpha Kappa Kappa, luncheon, June 12.
Phi Chi, luncheon, June 13.
Kings County Medical Society, dinner, June 15.

Nu Sigma Nu medical fraternity will hold a luncheon, June 12, at the Yale Club and not at the Waldorf-Astoria, as announced in THE JOURNAL May 11, page 1941, according to a notice from Dr. Arthur F. Warren, 667 Madison Avenue, New York, president of the New York Alumni Association. Dr. Francis Carter Wood, New York, will speak on "Changing Medicine" and Dr. Stuart Graves, Tuscaloosa, Ala., "The Fraternity." The alumni of the University of Minnesota Medical School will hold a dinner at 6 o'clock Wednesday evening, June 12, at the Brauhaus Restaurant, New York. Dr. Louis A. Hauser, 140 East Fifty-Fourth Street, New York, is chairman.

**Seminar on Physical Therapy.**—The eighth annual seminar of the Western Section of the American Congress of Physical Therapy will be held, June 3-4, at the Fairmont Hotel, San Francisco. The speakers will include:

Dr. Harry Glenn Bell, San Francisco, Treatment of Erysipelas by Ultraviolet Light.
Gerhard K. Rollefson, Ph.D., Berkeley, Calif., Nature and Chemical Effects of Ultraviolet Light.
John D. de C. H. Saunders, San Francisco, Infra-Red Photography.
Dr. Arthur Merton Bassett, San Francisco, The Postural Syndrome.
Dr. Alice Potter, San Francisco, Diathermy in the Treatment of Bronchitis and Bronchiectasis.
Dr. John R. Upton, San Francisco, Local Heating in Pelvic Pathology.
Dr. Erie Liljencrantz, San Francisco, Freezing in Malignancy.
Dr. Joseph C. Risser, Los Angeles, Differential Diagnosis and Treatment of the Lumbosacral and Sacro-Iliac Pathology.
Dr. Ottiveil W. Jones Jr., San Francisco, Types of Low Back Pain and Sciatica Found in Association with Dislocations of Intervertebral Disks.
Dr. Verne T. Inman, San Francisco, Anatomic Discussion of Subluxations of the Spine: Manipulative Correction.
Dr. Mayo H. Soley, San Francisco, Anxiety States and Their Physiologic Manifestations.
Dr. Ernest G. Lion, San Francisco, Physical Therapy in Psychiatric Practice.
Dr. Samuel F. Boyle, San Francisco, Orthoptics.
Dr. Charles I. Singer, Long Beach, N. Y., Role of Spa Therapy in Chronic Degenerative Diseases.
Dr. Lucile M. Eising, San Francisco, Pool Therapy for Arthritis.
Dr. Benjamin Paul Davies, Stanford University, Calif., Treatment of Injuries to the Soft Tissues.

**Committee on Revision of the Pharmacopeia.**—At the thirteenth meeting of the United States Pharmacopeial Convention in Washington, D. C., May 14-15, the following were elected as members of the Committee on Revision of the United States Pharmacopeia, 1940-1950:

Dr. Henry G. Barbour, New Haven, Conn.
Dr. Walter A. Bastedo, New York, N. Y.
George D. Beal, Ph.D., Pittsburgh, Pa.
Francis E. Bibler, B.S., Indianapolis, Ind.
Dr. Charles L. Brown, Merion Station, Pa.
Joseph B. Burt, Ph.D., Lincoln, Neb.
Dr. William B. Castle, Boston, Mass.
Clifford W. Chapman, Ph.D., Baltimore, Md.
Bernard V. Christensen, Ph.D., Columbus, Ohio.
E. Fullerton Cook, Pharm.M., Philadelphia, Pa.
Dr. Arthur C. DeGraff, New York, N. Y.
Dr. Marion S. Dooley, Syracuse, N. Y.
Dr. Carl A. Dragstedt, Chicago, Ill.
J. Leon Lascoff, Pharm.D., New York, N. Y.
Charles O. Lee, Ph.D., Lafayette, Ind.
Asa B. Lemon, Pharm.D., Buffalo, N. Y.
Dr. Perrin H. Long, Baltimore, Md.
Dr. Eli K. Marshall Jr., Baltimore, Md.
Dr. George W. McCoy, New Orleans, La.
Dr. Walter L. Mendenhall, Boston, Mass.
Hugh C. Muldoon, Sc.D., Pittsburgh, Pa.
Dr. Erwin E. Nelson, New Orleans, La.
E. L. Newcomb, Pharm.M., New York, N. Y.
Charles Leonard O'Connell, Pharm.D., Pittsburgh, Pa.
Justin L. Powers, Ph.D., Washington, D. C.
Andrew G. DuMez, Ph.D., Baltimore, Md.
Robert P. Fischelis, Pharm.D., Trenton, N. J.
Perry A. Foote, Ph.D., Gainesville, Fla.
Dr. Harry Gold, New York, N. Y.
Forest J. Goodrich, Ph.D., Seattle, Wash.
Lloyd E. Harris, Ph.D., Norman, Okla.
Thomas J. Hill, D.D.S., Cleveland, Ohio.
M. L. Jacobs, Ph.D., Chapel Hill, N. C.
Glenn L. Jenkins, Ph.D., Minneapolis, Minn.
Charles B. Jordan, D.Sc., Lafayette, Ind.
John C. Krantz Jr., Ph.D., Baltimore, Md.
Henry A. Langenhan, Ph.D., Mercer Island, Wash.
J. Allen Reeve, Ph.D., Richmond, Va.
Leon W. Richards, Ph.D., Missoula, Mont.
George C. Schicks, Ph.C., Upper Montclair, N. J.
Carl L. A. Schmidt, Ph.D., Berkeley, Calif.
A. John Schwarz, Ph.D., Memphis, Tenn.
Leonard A. Seltzer, Sc.D., Detroit, Mich.
Dr. Virgil E. Simpson, Louisville, Ky.
Dr. Isaac Starr, Philadelphia, Pa.
Frank O. Taylor, Ph.C., Detroit, Mich.
Dr. Soma Weiss, Boston, Mass.
Elmer H. Wirth, Ph.D., Chicago, Ill.
Heber W. Youngken, Sc.D., Boston, Mass.
Louis C. Zopf, Ph.G., Iowa City, Iowa.

## CORRECTION

**Shot in the Vermiform Appendix.**—Dr. E. P. Hummel, Sterling, Colo., calls attention to a misnomer in the heading of the clinical note by Dr. John R. Earl, St. Paul, in THE JOURNAL, May 11, page 1864. Number 6 shot were found, not BB shot, as implied in the heading. BB shot are considerably larger than number 6.

# Foreign Letters

## LONDON

*(From Our Regular Correspondent)*

April 20, 1940.

### Cranial Surgery at the Front

When the last war began we were quite unprepared for a military effort on such a gigantic scale. Now the danger has been foreseen and arrangements have been made in advance in the light of our experience of the last war. As previous letters have shown, this is true of the medical corps. The latest advance announced is a mobile unit for cranial surgery to operate as near the battle front as possible. Since the last war there have been many advances in technic, largely in the use of electrical apparatus, x-rays, diathermy and so on which will be made available. For cranial surgery the Royal Army Medical Corps has constructed a mobile neurosurgical unit which is self contained. The vehicle is a motor lorry which carries a separate engine and dynamo. The cable conveys the current to the operating room, where it is distributed to lighting, surgical diathermy, operation table heaters and suction pump. The current also charges a 12 volt accumulator for the electromagnet. The equipment includes two sets of instruments, two folding operating tables with special folding head rests, two folding instrument tables and modern anesthetic apparatus. Sterilization of water and instruments is done by oil stoves, and there is also a high pressure sterilizer for instruments and dressings.

The personnel traveling in the lorry includes a neurosurgeon, a neurologist, an anesthetist, two surgical assistants and two operating room nurses. The unit is designed to operate chiefly at casualty clearing stations but will be based on a parent base hospital for its reserve supplies. It carries sufficient material for several hundred neurosurgical operations and can thus remain in the forward area for weeks at a time.

### The Greatest Evacuation in History

At the outbreak of the war the greatest evacuation in history —the removal from London and other centers to places of greater safety from air raids of 1,270,000 persons in four days— was briefly described. At the Royal Society of Medicine Dr. J. A. Glover, medical officer of the Ministry of Health, devoted his presidential address to the Section of Epidemiology and State Medicine to the epidemiologic aspects of this evacuation. Plans began to be formed at the time of the Munich crisis. The country was divided into eighty-one evacuation areas, 1,100 reception areas, chiefly small towns and rural districts, and neutral areas. The number of evacuable persons was estimated at 3,644,000, of whom half were school children. It was expected that 80 per cent would avail themselves of the official machinery (the evacuation was entirely voluntary). Offers to receive 2,000,000 school children in private houses were received. The Ministry of Health arranged with the local authorities for increased hospital provision for infectious diseases in the reception areas. For expectant mothers obstetric areas were defined according to accessibility to lying-in hospitals, and 137 maternity homes containing 3,700 additional beds were provided for normal cases. Consultant obstetric services and hospital accommodations were provided for abnormal cases. Arrangements were made for the prompt isolation of cases of puerperal pyrexia. An agreement was made with the British Medical Association for the domiciliary treatment of evacuated children. The Medical Research Council organized two central and twenty-three subsidiary laboratories to augment existing facilities. In many areas water supplies, sewerage and drainage were organized.

Of the evacuable population only one third was willing to go and on August 31 and the three following days 1,270,000 went to the reception areas. Of this number 166,200 were mothers or other adults who accompanied 260,300 young children, 12,291 were expectant mothers and 734,883 were school children unaccompanied by their mothers. The remainder, apart from 5,000 blind and crippled persons, were teachers and other helpers. The school population of the reception areas was increased from 1,958,000 to 2,693,000.

The most imminent risk to those evacuated seemed to be the spread of poliomyelitis, diphtheria, scarlet and enteric fevers and dysentery. Diphtheria and scarlet fever had a high incidence in recent years and seemed likely to flare up when town carriers and country susceptibles mixed. But the incidence of infectious diseases in the first four months of the war was remarkably low. It was fortunate that evacuation took place at the beginning of September, one of the most healthful periods of the year as regards droplet infections, such as measles, whooping cough and influenza. The incidence of poliomyelitis was only a third and of diphtheria and scarlet fever only two thirds of that for 1938. The result bore out the soundness of the policy of dispersal in billets. All previous experience showed that concentration of children in camps would have given much less satisfactory results as regards infectious diseases.

### Fatal Mercurial Poisoning After Cystoscopy

From the London Hospital Mr. B. H. Page and Mr. Clifford Wilson report in the *Lancet* three cases of fatal mercurial poisoning after cystoscopy, in which mercuric oxycyanide was used. Two of the cases occurred in 1938 and it was these which suggested the cause of death in the other, which occurred in 1935. The symptoms are illustrated by the following case: A man aged 58 complained of abdominal pain and difficulty in micturition. A vesical calculus had been removed five years before. Cystoscopy was performed under local anesthesia and the bladder was found normal except for fine trabeculation. From 8 to 10 ounces (about 250 cc.) of a 1:4,000 solution of mercuric oxycyanide was run into the bladder and left there. Twenty-four hours later the patient was admitted to the hospital with abdominal pain and inability to pass urine. He passed 4 ounces (120 cc.) of dark colored urine three hours after the cystoscopy, after which he was completely unable to micturate. He was in considerable distress with sunken cheeks and a dry furred tongue, but the temperature was normal. There were lower abdominal distention and some tenderness in the hypogastrium. Catheterization yielded 18 ounces (530 cc.) of blood stained urine. Vomiting, bloody diarrhea and suppression of urine followed. The blood urea rose to 600 mg. per hundred cubic centimeters of blood and he died on the thirteenth day. The necropsy showed ulcers in the bladder and colon and cloudy swelling of the kidneys. Mercurial solutions are widely used in cystoscopy and at the London Hospital extend back thirty years. Poisoning from their use appears to be extremely rare, but it is possible that instances have escaped recognition. Other patients were examined cystoscopically at the London Hospital on the same day and with the use of the same solution with no ill effects observed. Page and Wilson suggest that in their cases idiosyncrasy to the drug, possibly combined with abnormal retention and absorption, may have caused the fatalities. Whether this was so or not, there is no doubt that the use of mercuric oxycyanide solution in cystoscopy is dangerous.

### The Effects on the Ears of Flying

Medical officers are studying the effects of war flying on the ears of pilots. Recent experiences show that modern high performance airplanes, with their capacity for fast climbing and fast diving, subject the ears of pilots to considerable strain. Those who are suffering from colds and make a high speed climb on interception duty may contract tympanic trouble, and methods for their protection are being considered. In the large bombing airplanes long periods of flying in intense cold have

been found to affect the ears of some of the crew. Also the noise of the engines may reduce their staying powers. Methods of silencing have been developed for civil as well as military machines.

## PARIS

*(From Our Regular Correspondent)*

April 20, 1940.

### International Medical Relations

The Association for the Development of Medical Relations recently held its annual meeting with Professor Tiffeneau, dean of the Faculty of Medicine of Paris, presiding. The chairman's address included the following statements: Persecutions, deportations, executions and brutal force cannot enslave thought. International cooperation in science as in all other activities implies confidence and good faith, qualities now undermined by unbridled propaganda, threats and treachery. The forces of destruction must be challenged by the forces of creative activity. French education needs ceaselessly to be improved and the doors of French hospitals and laboratories need to be widely opened. Paris has remained a center which attracts many. Not only exiled physicians and educators but many others desiring to work in an atmosphere of freedom have enrolled to continue their studies; also prominent foreigners have come to teach. On the other hand, France has sent its medical representatives into foreign countries, particularly into Latin America, with advantages to both sides. Professor Peck, the speaker said, visited Paris during the past year with the members of the International Postgraduate Assembly of North America, as well as another distinguished group of American physicians directed by Dr. Thomas D. Walker. The association had been founded in 1919 with the presence of many American physicians and counted many members in all countries. In 1926, when a French-Japanese center was founded in Tokyo, a representative of the medical profession was requested by the Japanese government. The relations thus established proved remarkably satisfactory. Since physicians in all countries have the same objective, namely to know truth in order to do good, and since medicine knows no political or ideologic frontiers, there is a pertinence in suggesting that medical attachés be added to the military and consular attachés representing the nation abroad. The speaker also called attention to the fact that Louis Dartigues, one of the founders of the Union médicale latine in 1912 and known and esteemed for his devotion to the idea of a worldwide medical cooperation, recently died.

### Carotid Sinus Enervation

The region of the carotid sinus, according to a recent paper of Lucien Léger, is not a simple vascular bifurcation. It is, above all, the point of departure for a series of reflexes with neurovegetative repercussions. Tschermak's test disclosed some of them, especially those related to the system that regulates blood pressure. The ends of the sinus nerve within the carotid gland are endowed with a chemical sensitivity which Dautrebande succeeded in dissociating from sensitivity to mechanical stimuli. The carotid gland seems to possess an endocrine function not yet sufficiently defined. Lauwers had shown that the favorable results obtained in epilepsy by surgical intervention on the carotid sinus depended more on the site where intervention occurred than on its extent. His conclusions were that intervention should not be directed to the walls of the artery but should endeavor to suppress directly the nerve that connects the carotid sinus with the neural axis. From this idea had sprung several technics for the ablation of the carotid gland. The surgical problem consisted in avoiding injury to the arterial bifurcation and to the carotid gland or its vessels. Lauwers also combined sections of the sinus nerve and that of the external carotid with ablation of the carotid gland in order to facilitate access to the sinus and to increase simultaneously the output of the two internal carotid nerves.

Léger, however, rejects the section of the carotid nerve, recently proposed by Cordier and Coulouma, as complex and perhaps illusory. He performs the enervation of the sinus nerve at the point where the nerve joins the bifurcation and not at some distance. He rejects chloroform and accepts ether but prefers local anesthesia. It is mandatory to infiltrate the outer carotid coat and the tissue comprised within the vascular carotid bifurcation with a procaine hydrochloride solution free from epinephrine. It is better to operate twice if a bilateral operation is involved. A good test of the success of the enervation is the hemorrhage induced by the section of the artery of the carotid gland. Additional tests consist in histologic controls and in examining digitally the sensitivity of the tissues to mechanical stimuli. Ablation of the carotid gland carries with it only insignificant and temporary modifications of arterial tension, but the danger of syncope is present. This can be prevented only by extreme operative care and ample infiltrations of anesthesia. This operation is indicated especially in epilepsy, also in transitory cerebral anemia attended by convulsive crises. Léger's statistics include eighty-two cases with fifteen cures (18.7 per cent) observed for at least ten years, twenty-three improvements (26.2 per cent), forty-three failures (53.9 per cent) and one death (1.2 per cent).

### Death of Eugène Apert

Dr. Eugène Apert, a physician known for his contributions to children's and hereditary diseases, died at an advanced age.

## BERLIN

*(From Our Regular Correspondent)*

April 12, 1940.

### Medicine on Wheels for Rural Communities

In the Danube region formerly belonging to Austria, a so-called health wagon has been put into use among the farming communities. It consists of an automobile in which the rear seats have been removed and a medicine chest built in containing medical instruments, a scale for weighing children and a card index of the mothers and children in the various villages. The physician is his own chauffeur. He is accompanied by a social welfare nurse. The service cares for infants and preschool children and offers advice to mothers similar to that given in maternity and children's welfare stations in cities. Children receive medical care from the time they are born to the fourteenth year. Particular attention is paid to rickets and digestive disturbances. The work is done in close cooperation with the physicians and hospitals of the district. Similar health vehicles are planned for other Austrian districts. The villages and settlements are visited in regular rotation, about every two weeks on the same day. The medical service is free.

### Psychopathologic War Reactions

Recently Dr. F. G. von Stockert reported to the medical society of Frankfort on the Main observations made in the psychiatric ward of the military garrison of Frankfort of the first 100 patients received in the first two months of the war. He compared these observations with those made in peace times and in 1914. Fewer alcoholic cases were found than in 1914. In the first week of the war two suicides and three deaths from emotional instability, due to anxiety, occurred. Similar psychopathic reactions have frequently been observed during the first few months when recruits were drafted for military training in peace times. Experiences shows that hysterical reactions do not begin to accumulate until after a war has been in progress for some weeks. These hysterias are largely monosymptomatic. In the treatment of these cases it is important to check its evolution; for example, not to allow mutism to become aphonia.

### Student Regimentation

Labor conscription has been imposed on all students, effective in 1940, according to Dr. Scheel, national student leader. Until they have completed their education and can be mobilized for active soldiering, students must do duty during the first three semesters in unloading freight trains carrying coal or foodstuffs, in agriculture and forestry, in aviation, in technical emergency aid and so on. Students are formed into groups of from thirty to forty men according to their curriculums and then assigned. These activities obviously have no relation to their studies. It is also emphasized that students will be rated according to their efficiency. "Useless parasites" will be severely dealt with.

Students will also be conscripted for propaganda purposes. Participation in present day political problems is made a student obligation. For that reason students must stress, for the duration of the war, the study of the history and culture of other nations, including England, in order to track down arguments that may be used against England.

### Race and Diabetes

H. Lemser recently compiled comparative data of various countries to determine what part the environment and what part race played in the diabetic picture. Diabetes is found in all races that have been sufficiently studied. Racial differences, no doubt, are determining factors in the incidence of diabetes; for example, in the case of the Jews. But this incidence is not easy of demonstration because of the lack of adequate information regarding environmental and hereditary factors and of non-European races. Of greater significance are the degree of gravity of the disease and its evolution. The former is essentially hereditable and scarcely modifiable by the environment. No definite theories can yet be formulated regarding the effect of race mixture on diabetes.

### Additional Regulations on Medicines

According to a new ministerial decree, liver preparations intended to combat pernicious anemia and other diseases may now be dispensed only on prescription. The same regulations apply to benzedrine and its salts and to medicines containing these drugs and to iodine compounds and their preparations, except that a new prescription is required each time. For reasons of economy during the war, tincture of iodine must be doubly diluted with alcohol unless the undiluted form is expressly called for by the physician. The content of boric acid in boric acid ointment has been reduced from 10 per cent to 3 per cent (THE JOURNAL, Dec. 30, 1939, p. 2436).

## AUSTRALIA

*(From Our Regular Correspondent)*

April 9, 1940.

### Blood Bank for Overseas Army

The Australian Red Cross Society's gift of a mobile blood bank to the second Australian Imperial Force will enable transfusion to be brought into use nearer the front line and much earlier than ever before. The unit has now been officially handed over to the army. The blood bank, for which £1,550 was collected throughout Australia, comprises a blood transport and refrigerating van which carries eighty bottles of stored blood, and a service vehicle providing facilities for sterilization, distillation of water, repair of transfusion apparatus and the collection of blood from donors.

### Early Tuberculosis in Army Recruits

In accordance with the decision of military medical authorities to carry out x-ray examinations of the chests of army recruits who will subsequently proceed overseas, the first batch were examined early this year. The technic employed was to photograph on 35 mm. film the shadow thrown on a fluorescent screen. Expedition was imperative, and 2,220 were examined in one day with the assistance of fifteen technicians and three record clerks. Examining teams consisting of a physician and a radiologist sat almost continuously for five days. Of a total of 6,775 recruits examined, 0.49 per cent were rejected on evidence obtained by this method. Some doubt was expressed by the radiologists as to whether the 35 mm. film was satisfactory in its present stage of development. Of 6,622 men examined on the miniature film, 365 were classified as doubtful, and when subsequently retaken on 17 by 14 inch film 342 were accepted and twenty-three rejected. Only ten were rejected on the miniature film alone. It was felt that a 4 by 5 inch photograph of the fluoroscopic shadow would be easier to examine, and the large number of retakes on 17 by 14 film would in this way be avoided.

### National Health Drive

A health education campaign through press, radio and cinema is part of the plan for a nationwide health drive conceived by the commonwealth and state health authorities in Australia. It has the support of local branches of the British Medical Association. The object of this educative campaign is to inform the public of the preventive and curative medical and health services available. It will also stress the importance to the nation of preserving a high individual health standard. The eradication of tuberculosis by uniform preventive and remedial measures in all states is another aim. Results of the x-ray examination of army recruits had shown that incipient tuberculosis was prevalent among apparently robust men to the alarming extent of one in every 200. This might justify the extension of x-ray examination to make it available also for civilians. Tuberculosis should not be a major health problem in Australia. Australia's sunshine and pleasant weather assist in curing lung disorders. We have adequate supplies of fresh foods, and living conditions are good. With the medical skill and technical equipment now available, there is no reason why an adequate coordinated effort should not stamp out tuberculosis within fifteen years. The problem of venereal disease, the relation of animal diseases to domestic health and the control of various epidemic diseases are included in the plan for coordinated action.

### UNIFORM REGISTRATION OF DOCTORS

Complete uniformity in the registration of medical practitioners, nurses, dentists, chemists, optometrists and veterinary surgeons throughout the commonwealth is also proposed. This, however, does not involve any radical alteration in existing conditions. At present conditions of practice in all these professions are similar in all states but uniform regulations would be advantageous.

## Marriages

BENJAMIN BRUCE LANGDON, Fayetteville, N. C., to Miss Helen Browne Bennett of Chevy Chase, Md., March 23.

ALBERT V. STOESSER, Minneapolis, to Miss Marie Druckrey of Green Bay, Wis., in Shawano, Wis., April 27.

EDWIN W. ROBERTS, Watertown, N. Y., to Miss Mildred Marie Miller in Philadelphia recently.

JOHN R. TALBOT, Richmond, Va., to Miss Anne Virginia Bellows of White Stone, March 10.

EDWARD STEPHEN STANLEY to Miss Elizabeth Holman, both of San Angelo, Texas, January 18.

BERNARD E. BOLOTOFF, Rockford, Ill., to Miss Mary Younkus in East Chicago, Ind., in March.

WAYNE REESER, Lubbock, Texas, to Miss Evelyn Clayton Craft of Dallas recently.

HUGH H. TROUT JR. to Miss Elizabeth Page Browne, both of Roanoke, Va., April 6.

JOHN B. BOURLAND to Miss Mabel Sanders, both of Dallas, Texas, January 17.

# Deaths

**George Alder Blumer** ● Providence, R. I.; University of Pennsylvania Department of Medicine, Philadelphia, 1879; L.R.C.P. and L.R.C.S., Edinburgh, Scotland, 1884; past president of the American Medico-Psychological Association, Boston Society of Psychiatry and Neurology and the New England Society of Psychiatry; member of the American Psychiatric Association; honorary member of the Royal Medico-Psychological Association of England, the Society of Mental Medicine of Belgium and the Medico-Psychological Society of Paris; corresponding member of the Society of Psychiatry of Paris; formerly lecturer and adjunct professor of insanity at the Albany (N. Y.) Medical College; superintendent of the Utica (N. Y.) State Hospital from 1886 to 1899; superintendent and physician in chief to the Butler Hospital from 1899 to 1922 and since 1922 emeritus superintendent; editor emeritus of the *American Journal of Psychiatry;* aged 82; died, April 25, in the Jane Brown Hospital of arteriosclerosis.

**Henry Clarke Coe,** Washington, D. C.; Harvard Medical School, Boston, 1881; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1882; M.R.C.S., England, 1884; professor emeritus of gynecology at the New York University College of Medicine, formerly known as the University and Bellevue Hospital Medical College, New York, where he was professor of gynecology from 1896 to 1915; past president of the American Gynecological Society; member of the Medical Society of the State of New York; one of the founders and governor from 1927 to 1930 of the American College of Surgeons; served during the World War; consulting gynecologist to the Bellevue, Woman's, Polyclinic, Beth Israel and Memorial hospitals, New York; co-author with Dr. Keating of "Clinical Gynecology," published in 1894; aged 84; died, April 20, of heart disease and arteriosclerosis.

**Thomas P. Farmer** ● Syracuse, N. Y.; Syracuse University College of Medicine, 1906; member of the House of Delegates of the American Medical Association from 1933 to 1935 and from 1937 to 1939; professor of clinical gynecology at his alma mater; fellow of the American College of Surgeons; on the staffs of the Syracuse Memorial Hospital, St. Joseph's Hospital, Syracuse Free Dispensary and the Syracuse Psychopathic Hospital; at one time health officer; aged 56; died, April 12, of carcinoma of the axilla.

**Henrietta Tucker Tanner,** Philadelphia; Bennett College of Eclectic Medicine and Surgery, Chicago, 1898; Woman's Medical College of Pennsylvania, Philadelphia, 1922; member of the Medical Society of the State of Pennsylvania; at various times on the staffs of the Northwestern General Hospital, Woman's Hospital and the Germantown Hospital; aged 63; died, March 9, of coronary occlusion.

**Laurence James Dervin,** Somerville, Mass.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1903; member of the Massachusetts Medical Society and the New England Pediatric Society; formerly teaching assistant in pediatrics at the Tufts College Medical School, Boston; aged 63; died, March 30, in the Somerville (Mass.) Hospital of heart disease.

**John M. Quigley,** Clearfield, Pa.; Baltimore Medical College, 1898; member of the Medical Society of the State of Pennsylvania; past president and secretary of the Clearfield County Medical Society; for many years medical examiner of the public schools; formerly president of the board of health of Clearfield; on the courtesy staff of the Clearfield Hospital; aged 65; died, March 17.

**Nelson Borst,** Poughkeepsie, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1890; member of the Medical Society of the State of New York; formerly member of the board of health and school board; consulting physician to the Vassar Brothers Hospital and St. Francis Hospital; aged 83; died, March 28, in Miami, Fla., of myocarditis.

**Charles Edgar Chandler,** Hamilton, Texas; Memphis (Tenn.) Hospital Medical College, 1908; member of the State Medical Association of Texas; served during the World War; city health officer; formerly county health officer; for many years member of the school board; medical superintendent of the Hamilton Sanitarium; aged 54; died, March 26, of coronary occlusion.

**Carl Kurtz,** Los Angeles; Bellevue Hospital Medical College, New York, 1889; fellow of the American College of Surgeons; at one time professor of gynecology at the University of Southern California School of Medicine; formerly member of the board of education and board of health; aged 71; died, March 2, in the California Hospital of chronic myocarditis.

**John Newton Boyce,** Poughkeepsie, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; member of the Medical Society of the State of New York; veteran of the Spanish-American and World wars; on the staff of the Vassar Brothers Hospital; aged 66; died, March 29, of coronary thrombosis.

**Thomas Twood Warham** ● Minneapolis; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1897; an Affiliate Fellow of the American Medical Association; formerly county physician; aged 73; died, March 27, of coronary sclerosis, diabetes mellitus and chronic pulmonary tuberculosis.

**Frederic Purdy Hollister,** Scranton, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the Medical Society of the State of Pennsylvania; past president of the Lackawanna County Medical Society; on the staff of the Scranton State Hospital; aged 67; died, March 26, of angina pectoris.

**Clifford James Ulshafer** ● Shenandoah, Pa.; Temple University School of Medicine, Philadelphia, 1930; fellow of the American College of Surgeons; surgeon in chief and chief of the staff of the Locust Mountain State Hospital; aged 38; died, March 1, in the Temple University Hospital, Philadelphia, of pneumonia.

**Raphael Frederick Medrick,** Port Jervis, N. Y.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; member of the Medical Society of the State of New York; on the staff of the Deerpark Hospital, where he died, March 21, of chronic nephritis and hypertrophy of the prostate.

**Leonard Ezra Curtice,** Buffalo; Niagara University Medical Department, Buffalo, 1897; member of the Medical Society of the State of New York; on the staff of the Millard Fillmore Hospital; aged 71; died, March 30, in the Buffalo General Hospital of coronary occlusion.

**William Angelo Sparks,** Birmingham, Ala.; Medical College of Alabama, Mobile, 1905; member of the Medical Association of the State of Alabama; veteran of the Spanish-American War; aged 64; died, March 29, in the Veterans Administration Facility, Tuscaloosa.

**Horace Edmund Schlemm,** Long Beach, Calif.; Jefferson Medical College of Philadelphia, 1886; at one time a member of the school board of Reading, Pa.; formerly on the staff of the Reading (Pa.) Hospital; aged 80; died, March 12, of cerebral hemorrhage.

**Olive Whitney Wheaton,** Huntington, N. Y.; Cornell University Medical College, New York, 1928; member of the Medical Society of the State of New York; on the staff of the Huntington Hospital; aged 43; died, March 2, of a streptococcic infection.

**Joseph Arthur Collie,** Pasadena, Calif.; Northwestern University Medical School, Chicago, 1898; for many years resident physician at the Las Encinas Sanitarium; veteran of the Spanish-American and World wars; aged 74; died, March 5, of miliary tuberculosis.

**Willis Johnson Middleton,** Acton, Mass.; Tufts College Medical School, Boston, 1901; assistant in anatomy at his alma mater from 1902 to 1905; for many years on the staff of the Quincy (Mass.) Hospital; aged 71; died, March 14, of heart disease.

**Wallace Harden Smith,** Natchez, Miss.; University of Tennessee College of Medicine, Memphis, 1929; member of the Mississippi State Medical Association; on the staff of the Natchez Sanatorium; aged 34; died, March 24, of anaphylactic shock.

**Byron O. Nobles,** Milwaukee; Northwestern University Medical School, Chicago, 1893; at one time professor of obstetrics at the Milwaukee Medical College; aged 76; died, March 23, of chronic myocarditis, arteriosclerosis and broncho-asthma.

**Charles Augustus Orr,** Excelsior Springs, Mo.; National University of Arts and Sciences Medical Department, St. Louis, 1913; member of the Missouri State Medical Association; aged 67; died, March 11, in Knoxville, Iowa, of duodenal ulcer.

**George Waldo Burgess,** Guerneville, Calif.; Cooper Medical College, San Francisco, 1895; veteran of the Spanish-American War; aged 70; died, March 7, in the Southern Pacific General Hospital, San Francisco, of carcinomatosis.

**John Anderson Bowles,** Tacoma, Wash.; Washington University School of Medicine, St. Louis, 1907; member of the Washington State Medical Association; served during the World War; aged 58; died, February 2, of a broken back.

**Richard Coleman Ditto,** Oakville, Iowa; Keokuk Medical College, College of Physicians and Surgeons, 1901; member of the Iowa State Medical Society; aged 66; died, March 28, in the Burlington (Iowa) Hospital of myocarditis.

**Forster Hanson Smith,** Lowell, Mass.; Harvard Medical School, Boston, 1902; formerly superintendent of the Lowell Tuberculosis Hospital; aged 62; died, March 17, of wounds of the throat and wrist self inflicted with a razor.

**Foster Harris Kennedy,** Wellsboro, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1911; member of the Medical Society of the State of Pennsylvania; aged 54; died, March 9, of pulmonary embolism.

**Samuel R. Phillips,** Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1905; member of the Medical Society of the State of Pennsylvania; aged 57; died, March 22, of coronary thrombosis and diabetes mellitus.

**Sidney Archer Lord,** Boston; Harvard Medical School, Boston, 1894; member of the Massachusetts Medical Society; formerly on the staff of the Massachusetts General Hospital; aged 70; died, March 30, of pneumonia.

**Solomon P. Hakes** ● Tioga, Pa.; University of the City of New York Medical Department, 1888; formerly secretary of the Tioga County Medical Society; bank president; aged 78; died, March 14, of arteriosclerosis.

**James Wooten Smith,** Poth, Texas; Medical College of Virginia, Richmond, 1901; member of the State Medical Association of Texas; aged 60; died, February 25, of injuries received in an automobile accident.

**Alvin Joseph Brah** ● Milwaukee; Wisconsin College of Physicians and Surgeons, Milwaukee, 1908; on the staff of St. Joseph's Hospital; aged 53; died, March 26, of chronic valvular heart disease and myocarditis.

**Mary Forrester Hobart,** Needham, Mass.; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1884; aged 88; died, March 21, of uremia due to cardiorenal degeneration.

**Archibald Carter Long,** Sheridan, Mo.; Ensworth Medical College, St. Joseph, 1900; aged 70; died, March 28, in the Missouri Methodist Hospital, St. Joseph, of pulmonary edema and arteriosclerotic heart disease.

**Henry David Hully,** Griswold, Iowa; University of Nebraska College of Medicine, Omaha, 1902; member of the Iowa State Medical Society; aged 68; died, March 23, of organic heart disease.

**John Daniel Hare,** Reedley, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1890; aged 82; died, February 3, of chronic cystitis, retention of urine and heart disease.

**Jean Harris Whitney Morse,** Redwood Falls, Minn.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1897; aged 67; died, March 27, of cerebral hemorrhage.

**Anna Samuilovna Wilner,** Rockaway Beach, N. Y.; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1895; aged 66; died, February 9.

**Elmer Howard Hankey,** Pittsburgh; College of Physicians and Surgeons, Baltimore, 1914; aged 51; died in March in the Western Pennsylvania Hospital of cirrhosis of the liver.

**James M. Gober,** Beaumont, Texas; Kentucky School of Medicine, Louisville, 1894; aged 74; died, March 21, in St. Therese Hospital of injuries received in an automobile accident.

**John George McFadden,** Loveland, Colo.; Western Reserve University Medical Department, Cleveland, 1894; aged 70; died, March 4, of carcinoma of the prostate and uremia.

**Edith Sturges Heller,** West Hartford, Conn.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1894; aged 73; died, February 29, of cerebral hemorrhage.

**Thomas Jefferson Turpin,** Chihuahua, Mexico; Kentucky School of Medicine, Louisville, 1869; Jefferson Medical College of Philadelphia, 1870; aged 92; died, March 5, of senility.

**Clarence Eugene Hight,** Pasadena, Calif.; Medical School of Maine, Portland, 1900; served during the World War; aged 65; died, March 15, of rheumatic heart disease.

**Monroe J. Polk,** New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1895; died, March 4, of coronary thrombosis.

**William Lewis Stephens,** Meridian, Calif.; Eclectic Medical Institute, Cincinnati, 1901; formerly county health officer; aged 67; died, March 18, of cerebral hemorrhage.

**Houston E. Snyder,** Glenns Ferry, Idaho; Western Eclectic College of Medicine and Surgery, Kansas City, Kan., 1909; aged 56; died, March 26, of heart disease.

**Denis Joseph McMahon,** Breckenridge, Minn.; College of Physicians and Surgeons, Keokuk, Iowa, 1894; aged 70; died, March 12, of carcinoma of the throat.

**Herbert R. Flint,** Hornell, N. Y.; University of Buffalo School of Medicine, 1882; for many years health officer; aged 86; died, March 28, of heart disease.

**Herbert Chester Thomas,** Altoona, Pa.; Jefferson Medical College of Philadelphia, 1915; aged 48; died, March 15, in the Mercy Hospital of osteomyelitis.

**John Kercher,** Chicago; Chicago Medical College, 1890; member of the Illinois State Medical Society; aged 77; died, March 20, of arteriosclerosis.

**Stephen Edwin Peters** ● Masontown, Pa.; Chicago College of Medicine and Surgery, 1909; aged 56; died, March 13, of coronary artery occlusion.

**Charles Abram Bosarth,** Mason City, Iowa; Hahnemann Medical College and Hospital, Chicago, 1886; aged 86; died, March 28, of myocarditis.

**Henry Beier,** Huntington Park, Calif.; St. Louis University School of Medicine, 1918; aged 46; died, February 23, of coronary thrombosis.

**James Henry Kelley,** Flemingsburg, Ky.; Hospital College of Medicine, Louisville, 1892; aged 69; died, March 22, of pernicious anemia.

**James A. Printy,** Flushing, N. Y.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1882; aged 85; died, February 12.

**Edward Lorne McIntyre,** High Prairie, Alta., Canada; University of Toronto Faculty of Medicine, 1911; aged 53; died, February 1.

**Thomas Erlin Kaiser,** Oshawa, Ont., Canada; Victoria University Medical Department, Coburg, 1890; aged 76; died, February 29.

**Henry W. Coffin,** Glens Falls, N. Y.; New York Homeopathic Medical College, New York, 1881; aged 80; died, February 17.

**James Mitchell Nairn,** Toronto, Ont., Canada; Victoria University Medical Department, Coburg, 1886; aged 81; died, February 12.

**Ernest Wilson McNiece,** Aylmer (West) Ont.; Western University Faculty of Medicine, London, 1918; aged 49; died, January 20.

**Paul Ewert,** Golden, B. C., Canada; McGill University Faculty of Medicine, Montreal, Que., 1912; aged 56; died, February 4.

**James Robertson,** Montreal, Que., Canada; Hahnemann Medical College and Hospital, Chicago, 1910; aged 62; died, February 5.

**Moses Sylvester Howell,** Greenville, Texas; University of Georgia Medical Department, Augusta, 1885; aged 77; died, March 8.

**Jacob Louis Rubinstein** ● New York; University of Maryland School of Medicine, Baltimore, 1904; aged 56; died, February 27.

**Jesse Sturgeon,** Salem, Ohio; Bellevue Hospital Medical College, New York, 1878; aged 86; died, March 13, of pneumonia.

**Clyde Loverne Gillam,** Rawlins, Wyo.; Marion-Sims College of Medicine, St. Louis, 1893; aged 67; died, February 28.

**Edmund Sanford Young,** Boston; Long Island College Hospital, Brooklyn, 1891; aged 84; died, January 20.

**William Elliott Bruce,** Cambridge, Ohio; Medical College of Ohio, Cincinnati, 1889; aged 78; died, February 24.

**Minnie Bell Chunn,** Electra, Texas; Gate City Medical College, Dallas, 1907; aged 64; died, February 9.

**William Gaylor,** Jellico, Tenn.; Tennessee Medical College, Knoxville, 1893; aged 73; died, March 13, of chronic nephritis.

**Erastus Robinson,** Shandon, Ohio; Miami Medical College, Cincinnati, 1876; aged 87; died, March 10, of senility.

**George Aloysius Murray,** Boston; Harvard Medical School, Boston, 1915; aged 55; died, February 21.

**Luther R. Burke,** Crowder, Miss. (licensed in Mississippi in 1911); aged 66; died, January 17.

# Correspondence

## PULMONARY EMBOLISM FOLLOWING THE INJECTION TREATMENT OF VARICOSE VEINS

*To the Editor:*—The unprejudiced reader of Dean and Dulin's paper "Pulmonary Embolism Following the Injection Treatment of Varicose Veins" (THE JOURNAL, April 6, p. 1344) can easily get the impression that the treatment of varicose veins by injections is not as safe as pictured by "numerous authors" who "report a low incidence of complications following the injection therapy of varicose veins," that "the dangers of this procedure are greater than is usually reported" and that high ligation or other surgical procedure reduces fatal embolism. Drs. Dean and Dulin base their conclusions on their experience with two fatal cases among 600 cases treated by injection; they imply that deadly embolism might have been avoided by a proper treatment explained in their conclusions 2, 3, 4, 5 and 6. The physician who wants to treat varicose veins or has to recommend a certain procedure should get an impartial picture of the value or disadvantage of the different methods. This picture could have been obtained here if, besides the fact of "low incidence of serious complications following the injection therapy of varicose veins," the observations and conclusions of the authors and papers cited would have been reported. Let me examine what they say:

According to Westerborn's Swedish statistics, the only ones available which differentiate between treatment of varicose veins by (*a*) different operations, (*b*) high ligation and consecutive injection and (*c*) injection alone, the following percentages resulted in deadly embolism: Of 6,994 cases in which operation was done eighteen, or 0.26 per cent, were fatal; of 1,200 cases in which high ligation of the saphenous vein and retrograde injection were done four, or 0.33 per cent, were fatal, and of 30,000 cases in which injection alone was done eleven, or 0.036 per cent, were fatal. These statistics show a ten times higher mortality rate in cases of ligation than in cases of injection.

Kettel says in his cited paper that the extremely low mortality rate in cases treated by injection can be further reduced by proper precautions. With regard to the high ligation and retrograde injection treatment of varicose veins, he states that the mortality rises up to from 0.5 to 1 per cent, citing Berntsen, Kilbourne, Laqua, Reichel and others. He wrote "The majority of the authors [Meissen, Kilbourne, Fraenkel, Gruca, Baur, Vigyázó] reject the combined treatment by high ligation and injection."

Probstein, reporting three nonfatal cases of embolism of his own observation, quotes in the cited paper 120,000 injections of varicose veins in 15,000 consecutive cases observed by Sicard and Gaugier without a single mortality.

Silverman wrote "A search of the literature has revealed a total of only nineteen cases of embolism following in hundreds of thousands of cases."

Kilbourne reports that he did not have a single death in his clinic among 20,000 injections of varicose veins. He wrote about the high ligation "This simple ligation has its disadvantages. Ligation may cause a funnel-shaped blind pocket in the vein proximal to the ligature in which the blood stagnates, allowing a thrombus to form, and this thrombus is not well attached to the vein wall as is the firmly inrooted thrombus formed by injection of highly irritating solutions. A mortality rate results which I have shown is 0.5 per cent in larger series. This is not inconsiderable in such a small operation." He further states that he ligates "only occasionally giant veins which resist the sclerosing effect of injection." In the majority of cases of giant veins he prefers not to ligate.

In consideration of world literature, which to a large extent rejects the surgical treatment of varicose veins, and in view of the impressive statistics, one should be careful in recommending a risky method, especially as routine procedure. Reports from other authors are on hand regarding successful treatment of varicose veins by high ligation and retrograde injection. The number of such cases is still small. Surgeons convinced of the superiority of the surgical treatment over the injection treatment may continue to treat their patients with surgical methods. They should publish both their good results and their failures. In my opinion (*M. Rec.* **149**:169 [March 1]-1939) embolism in the injection treatment of varicose veins can be reduced to an insignificant minimum. Effective and safe treatment of varicose veins and their sequelae requires experience, a proper technic and a suitable solution (*M. Rec.* **147**:307 [April 6] 1938; *Arch. Dermat. & Syph.* **41**:530 [March] 1940).

LUDWIG ISAAK, M.D., New York.

## STOMACH LAVAGE IN TUBERCULOSIS

*To the Editor:*—In THE JOURNAL, April 13, page 1478, Dr. Kantor registered a complaint that workers in general, and we in particular (Stadnichenko, Cohen and Sweany: Stomach Lavage in the Diagnosis and Control of Treatment of Tuberculosis, *ibid.*, February 24, p. 634), did not give credit to Dr. Levy and himself for their work on tubercle bacilli in stomach contents. In 1915 Levy and Kantor (Tubercle Bacilli in Stomach Contents, *Arch. Diagnosis* **8**:154 [April] 1915), seventeen years after the original work of Meunier was published (Bacilloscopie des crachats extraits de l'estomac pour le diagnostic de la tuberculose pulmonaire de l'enfant, *Presse méd.* **2**:81, 1898), observed tubercle bacilli in the gastric contents of a tuberculous patient and "succeeded in demonstrating the organisms in this fashion in two other cases." No history or x-ray, clinical and laboratory examinations were mentioned in the three cases other than a mere mention of the tubercle bacilli. Even the ages of these patients are not given. For the latter reason alone, if for no other, we cannot agree with Kantor that "Prof. I. H. Levy is entitled to full credit for the idea" of reporting results on adults. Their observation might have been of interest to them, but their report did not contribute to the scientific knowledge of tuberculosis.

HENRY C. SWEANY, M.D., Chicago.

## PEDIATRIC EMERGENCIES

*To the Editor:*—I have always had a great deal of regard for the writings of Dr. Joseph Brennemann. However, I am constrained to take exception to an opinion expressed in a recent special article, "Pediatric Emergencies" (THE JOURNAL, March 16, p. 956). In discussing the treatment of congenital atresia of the esophagus, Dr. Brennemann states "No child has ever lived, and with the consent of the parents one is justified in letting the child die without treatment." Granted that the prognosis is nil in these cases, that the posterior mediastinum is *terra incognita* as far as the surgeon is concerned and that any procedure in the posterior mediastinum is attended with formidable obstacles, nevertheless an attitude such as "letting the child die" has a defeatist and nonprogressive ring.

There are many procedures carried out at present which only fifty years ago would have appeared to be impossible. Practically every part of the human body has become by degrees and improvements in technic amenable to surgery—the abdomen, the brain, the vascular system, the nervous system, the lungs, the heart and why not finally that hidden area the posterior mediastinum?

Our task as physicians is to strive to maintain life against all odds and to aim at perfection in our work and nothing

short of perfection. If something appears hopeless and devoid of solution now, it may not be so in the future. There are too many such examples in the history of all sciences to enumerate.

MICHAEL A. BRESCIA, M.D., Queens, N. Y.

[Dr. Brennemann replies:]

*To the Editor:*—At the time my paper on pediatric emergencies was written, to my knowledge no child with congenital atresia had ever lived, and the duration of life was usually shortened by operation. On a recent trip to Minneapolis I saw, however, a baby that had been operated on three months before and was still living. In that case a gastrostomy had been done and a catheter had been passed some little distance beyond the pylorus, followed by a tying off of the lower end of the esophagus near the bifurcation of the trachea. I quite agree with Dr. Brescia that "our task as physicians is to strive to maintain life against all odds and to aim at perfection in our work and nothing short of perfection." Since the child on whom the operation I have just spoken of was performed may live for years and since an artificial esophagus can then be built, there is at least a hope that the child may live for a long time. There is probably no hope of ever connecting the upper and lower ends of the esophagus, as the lower end is usually very thin and atrophic. However, I quite agree, after seeing this child, that one should operate with the technic employed in this case or with some other procedure.

JOSEPH BRENNEMANN, M.D., Chicago.

## INHERITANCE OF ANATOMIC DEFECTS

*To the Editor:*—Anent the question of inheritance of anatomic defects, I suppose that we must go as far back as Sir Oliver Lodge, who said that when an organism is developed it proceeds to run down like a clock as its fund or protoplasmic energy is expended. He referred to species. Weismann is not commonly quoted as reporting lamarckian ideas, but the tendency toward degeneration may be passed on nevertheless. In a case in which a fortune depended on the bearing of a son, I operated on a patient in search for causes of sterility and found closed oviducts as a congenital condition. On one side I folded up the oviduct so that the fimbriated end split open longitudinally could be grafted on a part of an opened oviduct in or part of the lumen near the uterus. This was a success as far as securing pregnancy was concerned, but when the child was born its esophagus opened into the trachea. When nature plans degeneration of a strain, persistence of the tendency may remain if not transmission of a particular form of degeneration.

ROBERT T. MORRIS, M.D., Stamford, Conn.

## AIR EMBOLISM

*To the Editor:*—In THE JOURNAL of February 24 Dr. H. M. Weyrauch Jr. and Drs. F. B. Walsh and H. K. Goldberg report instances of air embolism which were not immediately fatal. It is precisely in these circumstances that the inhalation of 100 per cent oxygen is indicated for the rapid absorption of the nitrogen blocking the arteries and capillaries. This should serve to restore function more quickly and perhaps avert death. The basis for this view can be found in the literature on the modern treatment of caisson disease and in the following articles:

Fine, Jacob; Frehling, Stanley, and Starr, Arnold: Experimental Observations on Effect of 95 per Cent Oxygen on Absorption of Air from Body Tissues, *J. Thoracic Surg.* 4:635 (Aug.) 1935.

Schwab, R. S.; Fine, Jacob, and Mixter, W. J.: Reduction of Postencephalographic Symptoms by Inhalation of 95 per Cent Oxygen, *Arch. Neurol. & Psychiat.* 37:1271 (June) 1937.

Fine, Jacob; Hermanson, Louis, and Frehling, Stanley: Further Clinical Experiences with 95 per Cent Oxygen for Absorption of Air from Body Tissues, *Ann. Surg.* 107:1 (Jan.) 1938.

JACOB FINE, M.D., Boston.

# *Queries and Minor Notes*

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## HAZARDS FROM COMPETITIVE SPORTS

*To the Editor:*—How many deaths and how many serious injuries occur annually in connection with high school football games, and how many in connection with college football games? How do these fatal and nonfatal accident rates in football compare with corresponding rates in other popular games, such as baseball; and how with allegedly dangerous sports, such as sail plane gliding? (Figures for the last point presumably are to be found in German sport or military medical publications.) Comparison with other fighting games, such as rugby, hockey, ice hockey, polo, soccer and the English football would also be welcome. M.D., Texas.

ANSWER.—According to statistics for the nine years from 1931 to 1939 compiled by Dr. Floyd R. Eastwood, of Purdue University, there was a total of twenty-six deaths in nine years directly attributable to college football, and of 107 deaths attributable to high school football. The number is steadily diminishing. In 1931 there were eight college deaths, twelve high school; in 1939 three college deaths, seven high school. This gives a 63.6 per cent decrease in the number of fatalities directly associated with football. As the estimated number exposed to football for the nine years was 616,000 high school and 65,690 college players, this gives an incidence of deaths per hundred thousand of 1.86 and 4.37 respectively. The motor vehicle rate is 32.8 per hundred thousand for the same age group.

The injuries in high school football were 90.3 per thousand in 1935 (Eastwood).

In a review of a five year period from 1930 to 1934 at Northwestern University by Dr. Marcus H. Hobart there were 368 football injuries, seventy wrestling, fifty basketball, thirty-five baseball and thirty track. As nearly five or six times as many play football, the percentage of danger is about the same as in other sports. These statistics probably give an indication of the general average.

Statistics for allegedly dangerous sports as sail plane gliding as "presumably found in German sport or military medical publications" were not found, nor were those of rugby, hockey, soccer and English football.

## LARGE CODEINE DOSAGE

*To the Editor:*—Would 1 grain (0.065 Gm.) of codeine sulfate every half hour for eight consecutive doses (8 grains [0.5 Gm.] in four hours) be considered a lethal dose for an average normal woman? What is considered a minimal lethal dose of codeine for an adult, if there is any such thing? I am not including drug addicts or people who have been in the habit of taking narcotics of any kind for some length of time. If a person had taken an overdose of codeine, sufficient to cause death, what would the autopsy show? In a case of this kind, on receipt of such a prescription, what is the medicolegal responsibility of the pharmacist to the physician and to the patient? M.D., Ohio.

ANSWER.—This dosage of codeine sulfate would not be considered lethal for an average normal woman; a fatal result would be exceptional; indeed, a fairly comprehensive search of reference books fails to reveal any reports of fatal codeine poisoning. Flury and Zangger (Lehrbuch der Toxikologie, Berlin, Julius Springer, 1928, p. 282) state that doses up to 1 Gm. cause inconvenience rather than danger to life. S. Weir Mitchell took 5 grains (0.32 Gm.) without alarming symptoms (Wood, H. C.: Therapeutics: Its Principles and Practice, ed. 11, Philadelphia, J. B. Lippincott Company, 1902, p. 137). The British Pharmaceutical Codex states that "large doses are sometimes given, up to 3 decigrams [5 grains] three times daily." However, the symptoms may be fairly alarming: Lewin (Gifte und Vergiftungen, Berlin, Georg Stilke, 1929, p. 632) cites a case in which "0.8 Gm. resulted in muscular weakness, miosis, vertigo, mild delirium, clonic spasms, fast pulse, then collapse." In another case, cited by Kobert (Intoxikationen, Stuttgart, Ferdinand Enke, 1906, p. 999), 0.5 Gm. (8 grains) produced restlessness, reddening of the skin and conjunctivas, mild muscle twitchings, slowed pulse, slow respiration and widely dilated pupils. Recovery resulted after artificial respiration, gastric lavage and analeptics. The mydriasis persisted for several days. Necropsy would presumably show asphyxia. When the dose is unusually large it would be advisable for the pharmacist to check with the physician before delivering the prescription.

## BLOOD AND ALBUMIN IN URINE

**To the Editor:**—Does the occurrence of albumin in a specimen of urine in which blood is found present here any significance as to whether the bleeding is from a surgical lesion in the urinary tract or from a so-called medical nephritis? If it has such significance is there any absolutely positive method of determining whether the albumin is coming from a nephritic process or is merely accompanying the surgical bleeding?

U. S. Hargrove, M.D., Baton Rouge, La.

ANSWER.—Plasma protein is practically always present in urine containing blood. Hence the occurrence of proteinuria cannot by itself be used to distinguish between medical and surgical diseases of the kidney or lower urinary tract. It is only in case of slight microscopic hematuria due to urinary calculus or other surgical lesions that the ordinary clinical tests for albuminuria may yield a negative result. Under these circumstances persistent slight hematuria without proteinuria speaks strongly against the common medical diseases of the kidney but does not indicate the precise source of the bleeding in the urinary tract.

However, the quantity of protein in the urine is an important aid in differential diagnosis. A concentration of 0.2 per cent of protein (by weight) in urine containing little or no gross blood rarely occurs in the ordinary surgical lesions of the urinary tract. When the proteinuria reaches a value of 0.4 or 0.5 per cent the probability is strong that one is dealing with some diffuse renal process or severe circulatory disturbance. In the presence of gross hematuria the protein estimation should be made on the supernatant protein of the centrifuged urine. A little calculation would show that considerable hemorrhage into the urinary tract is required to raise the concentration of plasma protein in the urine to 0.3 or 0.4 per cent. On the other hand, a slight leakage of protein into each or most of the glomerular capsules can readily result in several grams of protein in the twenty-four hour urine, because of the great number of glomeruli and the inability of the tubules to reabsorb the large protein molecules. Therefore much albuminuria may be present with little or no demonstrable hematuria in diffuse medical lesions of the kidney. Even in focal nephritis there is usually more protein in the urine than one would expect from the amount of blood found. Occasionally, in the subsidence of acute glomerulonephritis, miscroscopic hematuria may be observed without proteinuria.

While there is no single absolutely positive method of differentiating between the albuminurias of medical and surgical renal processes, the symptoms, the presence of erythrocytes and other casts in the urinary sediment, the level of renal function and the results of cystoscopy or pyelography should make it possible for the physician to arrive at an accurate diagnosis in nearly all cases.

## DIABETES AND HYPERTENSIVE DISEASE

**To the Editor:**—A man aged 32, weighing 185 pounds (84 Kg.), 5 feet 10 inches (178 cm.) in height, working underground as a miner, during the past two months noticed that his weight was going up, that his face was becoming bloated and red, that his appetite was tremendous, that thirst was considerable and that he passed abnormally large amounts of water, especially at night. The last few weeks he has had severe giddiness and slight headache and weakness. He was large and flabby looking, red faced and puffy around the eyes, extremely nervous and apprehensive. There were several decayed teeth, the heart was slightly enlarged to the left, the pulse was rapid (90) the blood pressure was 260 systolic, 130 diastolic, and the patellar reflexes were absent. Examination revealed a specific gravity ranging from 1.014 to 1.026, albumin negative, twenty-four hour samples of urine ranging from 10 to 20 Gm., numerous granular and pus casts, a few red cells and no bacteria. The dextrose tolerance test was fasting 80 mg., first hour 131 mg., second hour 145 mg. and third hour 130 mg. This test was taken after the patient had been on a diabetic diet for one week. Blood urea nitrogen was 14 mg., blood urea 23.6 mg., and blood uric acid 1.8 mg. Repeated blood counts did not reveal anemia, leukocytosis or any other abnormality. The blood Wassermann reaction was negative. A tentative diagnosis of mild diabetes complicated by a nonspecific chronic nephritis was made and the patient was put on a modified diabetic-nephritic diet of 2,500 calories at bed rest with a limitation of sugars and a moderate amount of protein. The bad teeth were removed, a preparation of theobromides and phenobarbital and crystoral tetramizole were used as drugs, and moderate amounts of insulin (20 units daily in divided doses with poor tolerance and a slight reaction) but the patient does not seem to improve and the blood pressure is going up. Is the diagnosis correct? Can you suggest further treatment? Can a chronic nephritis spill as much as 20 to 30 Gm. of dextrose in twenty-four hours in the urine? The symptoms at first suggested purely a diabetic condition but the signs tend more to a nonspecific chronic nephritis. Incidentally the patient's temperature has always remained normal. He still has the symptoms of polyuria, polydipsia and polyphagia. M.D., Idaho.

ANSWER.—There would seem to be nothing amiss with the diagnosis of diabetes in this case. The clinical symptoms and the laboratory observations clearly warrant such a diagnosis. The dextrose tolerance curve is that of diabetes, although not severe. The occurrence of a blood pressure of 200/130 in a 32 year old man is not part of diabetes. This indicates the additional presence of hypertensive disease. The evidence of nephritis is not good, as cylindruria and hematuria are not infrequently encountered in diabetes. In order to clear up some obscurities in this case one must determine whether any feature of the hypertensive disease might produce glycosuria. First one must consider the possibility of a cerebral hemorrhage in the region of the fourth ventricle. This seems unlikely, as other signs of cerebral hemorrhage are lacking and this glycosuria is persistent. Second, one must consider the presence of an adrenal tumor. Certain adrenal medullary tumors could produce both hypertension and glycosuria. These are rare but certain features of this case arouse suspicion. The easily controlled but persistent hyperglycemia, the rising blood pressure and the hematuria are suggestive circumstances. Such a diagnosis is not easy to confirm. X-ray examination will sometimes reveal the tumor. Pyelograms are sometimes helpful and occasionally the tumors may be palpated.

If these possibilities fail of proof, it would seem wise to treat the patient as hypertensive with mild diabetes and not treat the diabetes too vigorously with insulin.

## PINWORMS, HEXYLRESORCINOL AND DEATH

**To the Editor:**—A normal boy aged 4 years in good health had pinworms. Having had no breakfast, at 9 a. m. he received 0.4 Gm. of hexylresorcinol (caprichol). A cleansing soapsuds enema was given and returned with good results. At 10:15 1 pint of hexylresorcinol solution (1:1,000) with 8 ounces of warm water was given as an enema. After being retained for seven minutes it was expelled. At 10:30 the boy complained of epigastric pinings and headache, which quickly became severe, with vomiting brought up remains of the medication. Coma and convulsions appeared, which seemed to affect the left side of the body more. The child was immediately hospitalized. On admission he was comatose and pale, with frequent severe convulsions of all extremities. The temperature was 97 F., respiratory rate 10, pulse rate 120. The pupils were widely dilated and did not react to light. The right was larger than the left. Both optic disks were blurred. No neck rigidity or Brudzinski sign was present. The ears, nose, throat, heart and lungs were normal. Some slight cervical adenopathy was present. The abdomen was distended moderately. The right Babinski sign was extensor. There were no other positive neurologic symptoms. The blood count on admission was 5,400,000 red blood cells, 105,000 white blood cells, 84 per cent polymorphonuclears, no eosinophils, 12 per cent lymphocytes and 4 per cent monocytes. The Schilling index was not done, but no abnormally early polymorphonuclears were seen. The spinal fluid pressure was increased. Fifteen cc. was withdrawn, three tubes all equally normal and clear. The urine was not obtained. Phenobarbital was given hypodermically, ether to control convulsions, bromide and chloral by rectum. Gastric lavage was done and magnesium sulfate was passed through a stomach tube. Oxygen and infusions were given. Convulsions recurred with diminishing frequency and intensity. The child thus reacted slightly at about 3 p. m. The temperature was 104 F., pulse rate 140, respiration rapid and irregular. The coma was not as deep and the boy was able to sit himself in the bed. The pupils were still dilated and the disks blurred. Abdominal distention was less and the right Babinski reflex was gone. This condition continued until 6 o'clock (eight hours from the onset of symptoms), when the patient vomited blood and passed some blood rectally, developed pulmonary edema and died. Autopsy showed cerebral edema, slight congestion of the mucous membranes of the stomach and small intestine and acute congestion. Can you assist us in the solution of the following problems? Have cases of severe hexylresorcinol poisoning been reported before? What clinical pictures have they presented in the mild and severe forms? How could one have tested sensitivity before treatment? Can hexylresorcinol decompose to form a poisonous by-product? Does the white count of 105,000 point to a sensitivity reaction even though there is absence of eosinophilia? M.D., N. Y.

ANSWER.—In answering this inquiry regarding death following the use of hexylresorcinol in a case of pinworm infestation, it is impossible to account for the signs and symptoms observed. Hexylresorcinol is a local irritant, it is slowly absorbed, and about 20 per cent of it is excreted in the urine. No record has been found of systemic poisoning from hexylresorcinol in spite of its having been given in large amounts to many thousands of persons. One would not believe that the child could have died from a gastrointestinal hemorrhage; neither could the child have died from decomposition of hexylresorcinol in the body, as practically all of the hexylresorcinol after oral administration has been accounted for by finding it in the urine and stools. The lower members of any series of phenols may cause convulsions after absorption, but these are not seen with higher members of the series, and in toxicity experiments with hexylresorcinol no convulsions were seen. The dose of hexylresorcinol given to the child is a common therapeutic dose. There is nothing in this case which would indicate intoxication from hexylresorcinol.

As the description is read "1 pint of hexylresorcinol solution (1:1,000) with 8 ounces of warm water was given as an enema." If this hexylresorcinol solution was the commercial S. T. 37, this would have contained approximately 150 cc. of glycerin, which well might have caused collapse from local irritation and removal of water, but even this could not account for the fever, white count and convulsions, except that it is well known among pediatricians that any severe poisoning may show a remarkable symptom complex in children.

The cause of death of this child remains unexplained.

## PERSISTENT INTERCOSTAL NEURALGIA

**To the Editor:**—A woman aged 59 has had neuralgia involving the left fifth, sixth, seventh and eighth intercostal nerves since Aug. 6, 1937, at which time the pain set in suddenly. The red and white blood cells and the hemoglobin are normal. The blood Wassermann reaction is negative. Physical examination is entirely negative except for the specified nerves. The patient has received two nerve blocks of the involved nerves with no result. She has also received roentgen therapy, stovaine carvacol, thiamin chloride and short wave therapy, without good results. She has had to take from four to six capsules daily containing morphine sulfate or pantopon or dihydrol, plus acetylsalicylic acid, in spite of which it has been necessary to give her from one-fourth to one-half grain morphine sulfate hypodermically two or three times a week. She has not been free from pain since the onset for longer than four days at a time. Two neurosurgeons have told that direct attack on the involved nerves is indicated. Is there anything else I can offer the patient before subjecting her to this formidable step? Leon A. Frankel, M.D., Philadelphia.

Answer.—Neuralgia of the type described is often perplexing to treat; drug treatment usually is ineffective and a large number of such patients eventually seek surgical relief from both the pain and the heavy doses of drugs. Without some such treatment which will, by anatomic interruption, abolish the pain unquestionably, the disturbance may continue unabated for an indefinite time and, since no specific lesion exists, any attempt at direct therapy, other than surgical, is usually futile.

Following the suggestions of Leriche, a procainization of the sympathetic ganglion of the corresponding segments might be attempted. This is a procedure requiring much skill, and an inaccurate injection frequently leads to the opinion that such treatment is without merit. Such an injection failing, and considering the treatments already tried, posterior rhizotomy, sympathetic ramisectomy or even chordotomy (low cervical or high thoracic in this case) are the three surgical measures of most promise. Of these three, chordotomy is the only one which need be considered a "formidable step," and it can be safely done by an experienced neurosurgeon.

## INTESTINAL ADHESIONS AND PAIN

**To the Editor:**—A young married woman has had four laparotomies, the last one a sympathectomy for severe dysmenorrhea. She is now suffering from severe attacks of abdominal pain resulting from what appear to be numerous intestinal adhesions. What form of therapy do you suggest for treating the adhesions and the attacks of pain? M.D., New Jersey.

Answer.—This is a difficult problem. One must first be certain that all other causes of abdominal pain have been excluded before the diagnosis of intestinal adhesions is made. The urinary tract should be carefully studied as well as the gallbladder, stomach and duodenum. Diaphragmatic hernia should be excluded. If it seems that intestinal adhesions most likely explain the attacks of pain it would be well to try to take flat x-ray plates of the abdomen in the horizontal and vertical positions to see whether there are single, distended loops. Usually it is unwise to do any operation for adhesions unless frank intestinal obstruction occurs. Occasionally, however, if there is a definite inflated loop which can be identified by x-ray examination at the time of the maximum pain, a minimal type of operation to free the offending adhesions may be of value. In this event it is worth trying to use some amniotic fluid concentrate after the operation.

If operation is not carried out and the pain persists, a mild sedation must be given. It is desirable to avoid narcotics because of the habit-forming tendency.

Finally, one should be sure there is not an improper evaluation of pain because of psychiatric disturbance.

## REACTIONS FROM SOLUTIONS USED FOR OBLITERATING VEINS

**To the Editor:**—I am eager to know whether there is any medical literature supporting the conclusion that erythema multiforme may be caused by the various or any specific chemical used in the injection treatment of hemorrhoids. Guthrie H. Wisner, M.D., Richmond, Ind.

Answer.—Sensitization to solutions used for obliterating veins has been observed repeatedly. Apparently Ritchie (*Edinburgh M. J.*, November 1933, p. 157) was the first to call attention to these reactions. He described the following three types: (1) erythematous patches on the skin, (2) gastrointestinal disturbances with abdominal pain and diarrhea appearing shortly after the injections, and (3) pain across the back followed by collapse, cyanosis, fall in blood pressure and temporary loss of consciousness. This severe "nitritoid" reaction may closely resemble pulmonary embolism. The erythematous patches are the most frequent type of sensitization and have been seen after the use of quinine, salicylates and sodium morrhuate and even after solutions of sugar if they contain nitrogenous impurities. A partial list of references may be consulted:

Dermatitis from Invert Sugar for Varicose Vein Injections, Queries and Minor Notes, The Journal, May 21, 1938, p. 174.
Prayer, L. L., and Becker, S. W.: Sensitization Phenomena Following Use of Sodium Morrhuate, *ibid.*, March 21, 1935, p. 907.
Zimmerman, L. M.: Allergic-like Reactions from Sodium Morrhuate in Obliteration of Varicose Veins, *ibid.*, April 14, 1934, p. 1216.
Lewis, K. M.: Anaphylaxis Due to Sodium Morrhuate, *ibid.*, Oct. 17, 1936, p. 1298.

## PSYCHIATRY

**To the Editor:**—Does psychiatry include the study of criminal psychology, child psychology, correction of wayward adolescents and sexual disturbances besides the study of the insane? How can an individual obtain adequate training in these branches and what are the future possibilities of these branches in the medical field? Will a residency in a state institution give an individual sufficient background to carry on such studies?

M. S. Budich, M.D., East Bangor, Pa.

Answer.—The field of psychiatry should include the study of criminal psychology, the psychology of children, the correction for boys of the wayward adolescence, disturbances of the function of sex and, further, the study of the insane.

Adequate training in these branches should include internal medicine, neurology and psychiatry. To be a psychiatrist of merit requires more than an internship in a state hospital.

The future possibilities in psychiatry are similar to those which existed in surgery when Lister made his first antiseptic spray.

## ANIRIDIA

**To the Editor:**—A white girl baby aged 6 months was brought to me because the mother did not think the child could focus her eyes. The baby is perfectly normal in every respect except for the eyes, the rudimentary iris being represented by a thin black line around the edge of the cornea. There are no corneal opacities and both retinas appear normal. I have been able to find but little in any of my books on aniridia. Please let me know the relative frequency of this condition, the treatment, and the prognosis as to useful eyes in this patient. Any information relative to this condition will be appreciated.

W. Hill McCanless, M.D., Union Springs, Ala.

Answer.—There is an extensive literature dealing with aniridia. It is discussed in the second volume of the Textbook of Ophthalmology by Duke-Elder, 1938, page 1298. Other references, possibly not so comprehensive, are to the Kurzes Handbuch der Ophthalmologie, by Seefelder, volume 1, page 562; and the Eye and Its Diseases, by Berens, 1936, page 624.

## OVERWEIGHT YOUNG GIRL

**To the Editor:**—A 9 year old girl was brought to me because of overweight and enuresis. Her history and examination are negative except for obesity and dorsal padding of the fingers. The basal metabolic rate taken last year was normal. Her height is 57½ inches (146 cm.) and weight 123¾ pounds (56 Kg.) My diagnosis is preadrenal pituitary obesity. My plan is to give her small doses of thyroid daily and injections of solution of posterior pituitary biweekly. My questions are: Are there any better pituitary extracts for this purpose now on the market? Is twice a week often enough to give the injections or should they be given daily? Norman P. Bridge, M.D., Clinton, Conn.

Answer.—The most important therapeutic procedure is the administration of a well balanced weight reducing diet. This should be adequate in everything except calories. It may be supplemented with small doses of desiccated thyroid (as much as 1 grain [0.06 Gm.] of the U. S. P. material daily), but the main problem is dietary. There is no good evidence that solution of posterior pituitary is of value in the treatment of obesity. Moreover, there is no extract of the anterior lobe of the pituitary that is effective in this disorder.

## HOLLYHOCK POLLEN INSECT POLLINATED

**To the Editor:**—Please state specifically whether hollyhock pollen is wind borne or insect borne. I do not find a specific statement about this matter in any book on allergy at my disposal, although the general statement is made that the usual garden flowers produce insect borne pollen, listing rose, sunflower, cosmos, aster, dandelion and goldenrod.

M.D., Kentucky.

Answer.—Not only hollyhock but all members of the mallow family are strictly insect pollinated. A reference to three members of this family in the genus Hibiscus will be found on page 181 of Scheppegrell's "Asthma and Hay Fever," Philadelphia, Lea & Febiger, 1922.

# Medical Examinations and Licensure

## COMING EXAMINATIONS

### NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the National Board of Medical Examiners and Special Boards were published in THE JOURNAL, May 18, page 2052.

### STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 18-20. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, Sept. 3. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: *Basic Science*. Tucson, June 18. Sec., Dr. Robert L. Nugent, University of Arizona, Science Hall, Tucson. *Medical*. Phoenix, July 2-3. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Medical* (Regular). Little Rock, June 6-7. Sec., Dr. D. L. Owens, Harrison. *Medical* (Eclectic). Little Rock, June 6-7. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), Los Angeles, July 15. *Written examinations*. San Francisco, June 24-27. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

COLORADO: *Basic Science*. Denver, May 28-29. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver. *Medical*. Denver, July 3-6. *Applications must be on file not later than June 17*. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science*. New Haven, June 8. Chairman State Board of Healing Arts, Dr. Charles M. Bakewell, 1895 Yale Station, New Haven. *Medical. Written*. Hartford, July 9-10. *Endorsement*. Hartford, July 23. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic*. Derby, July 9-10. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination*. Dover, July 9-11. *Reciprocity*. Dover, July 16. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science*. Washington, Oct. 21-22. Sec., Dr. George C. Ashland, 201 District Bldg., Washington.

FLORIDA: Tampa, June 17-18. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Joint-Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

IDAHO: Boise, Oct. 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, June 25-27. Acting Superintendent of Registration, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 18-20. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

IOWA: *Medical*. Iowa City, June 4-6. *Basic Science*. Des Moines, July 9. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

KANSAS: Kansas City, June 18-19. Sec., Board of Medical Registration and Examination, Dr. J. P. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, June 6-8. Sec., Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Augusta, July 2-3. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Medical*. Baltimore, June 18-21. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic*. Baltimore, June 18-19. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, July 9-11. Sec., Dr. Stephen Rushmore, 413-P State House, Boston.

MICHIGAN: Ann Arbor and Detroit, June 12-14. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science*. Minneapolis, June 4-5. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical*. Minneapolis, June 18-20. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: Jackson, June. Asst. Sec., Dr. R. N. Whitfield, Jackson.

MISSOURI: St. Louis, June 6-8. Sec., State Board of Health, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

MONTANA: *Reciprocity*. Helena, Sept. 30. *Written*. Helena, Oct. 1-2. Sec., Dr. R. Cooney, 216 Power Block, Helena.

NEBRASKA: *Medical*. Omaha, June 12-14. *All applications must be on file 15 days prior to date of examination*. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

NEVADA: *Reciprocity with oral examination*. Aug. 5. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW JERSEY: Trenton, June 18-19. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 7-8. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York and Syracuse, June 24-27. Chief, Bureau of Professional Examinations, Mr. Herbert J. Hamilton, 315 Education Building, Albany.

NORTH DAKOTA: Grand Forks, July 2-3. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: Columbus, June 3-6. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA: Oklahoma City, June 5-6. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: *Medical*. Portland, June 18-20. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland. *Basic Science*. July 6. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: *Written*. Philadelphia and Pittsburgh, July 9-11. *Bedside*. Philadelphia, July 12-13. Dir., Bureau of Professional Licensing, Dr. James A. Newpher, 358 Education Bldg., Harrisburg.

PUERTO RICO: San Juan, Sept. 3. Sec., Dr. O. Costa Mandry, Box 3834, Santurce.

RHODE ISLAND: Providence, July 11-12. Sec., Division of Examination, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 25. Sec., Dr. A. Earle Bonzer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Rapid City, July 16-17. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

TENNESSEE: Knoxville, Memphis and Nashville, June 14-15. Sec., Dr. H. W. Qualls, 130 Madison Ave., Memphis.

TEXAS: San Antonio, June 17-19. Sec., Dr. T. J. Crowe, 918-20 Mercantile Bldg., Dallas.

VERMONT: Burlington, June 11-13. Sec., Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, June 18-20. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WASHINGTON: *Basic Science*. Seattle, July 11-12. *Medical*. Seattle, July 15-17. Sec., Department of Licenses, Mr. Nelson N. Vaughen, Olympia.

WEST VIRGINIA: Huntington, July 1-3. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: *Basic Science*. Milwaukee, June 1. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee. *Medical*. Milwaukee, June 25-26. Sec., Dr. E. C. Murphy, 314 E. Grand Ave., Eau Claire.

WYOMING: June 2-4. Sec., Dr. M. C. Keith, Capitol Bldg., Cheyenne.

## Wyoming February Report

Dr. M. C. Keith, secretary, Wyoming State Board of Medical Examiners, reports the written examination held at Cheyenne, Feb. 14, 1940. The examination covered twelve subjects and included eighty-two questions. An average of 75 per cent was required to pass. Four candidates were examined, all of whom passed. One physician was licensed by endorsement. The following schools were represented:

| School | PASSED | Year Grad. | Per Cent |
|---|---|---|---|
| Loyola University School of Medicine | | (1939)* | 79.2 |
| Creighton University School of Medicine | | (1933) | 79.1 |
| University of Nebraska College of Medicine | | (1938) | 77.6 |
| Jefferson Medical College of Philadelphia | | (1938) | 78.5 |

| School | LICENSED BY ENDORSEMENT | Year Grad. | Endorsement of |
|---|---|---|---|
| College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois | | (1905) | Illinois |

* This applicant has completed four years' medical work and will receive the M.D. degree on completion of internship. License has not been issued.

## North Dakota January Report

Dr. G. M. Williamson, secretary, North Dakota State Board of Medical Examiners, reports the written examination held at Grand Forks, Jan. 2-5, 1940. The examination covered thirteen subjects and included 100 questions. An average of 75 per cent was required to pass. Eight candidates were examined, all of whom passed. Two physicians were licensed by reciprocity. The following schools were represented:

| School | PASSED | Year Grad. | Per Cent |
|---|---|---|---|
| Northwestern University Medical School | | (1938) | 79.6 |
| Rush Medical College | | (1937) | 84.7 |
| Univ. of Minnesota Med. School | (1924) 85, (1929) 80.5, | (1939) | 78, 80.5 |
| University of Oregon Medical School | | (1936) | 80.4 |
| University of Pennsylvania School of Medicine | | (1936) | 81 |

| School | LICENSED BY RECIPROCITY | Year Grad. | Reciprocity with |
|---|---|---|---|
| Rush Medical College | | (1914) | Illinois |
| Creighton University School of Medicine | | (1921) | S. Dakota |

## Vermont February Examination

Dr. W. Scott Nay, secretary, Vermont State Board of Medical Registration, reports the written examination held at Burlington, Feb. 13-15, 1940. The examination covered twelve subjects and included ninety questions. An average of 75 per cent was required to pass. Four candidates were examined, three of whom passed and one failed. The following schools were represented:

| School | PASSED | Year Grad. | Per Cent |
|---|---|---|---|
| Cornell University Medical College | | (1938)* | 86.7 |
| University of Vermont College of Medicine | | (1939)* | 86.2 |
| Medizinische Fakultät der Universität, Wien | | (1926)* | 86.3 |

| School | FAILED | Year Grad. | Number Failed |
|---|---|---|---|
| Universidad Central de España Facultad de Medicina, Madrid | | (1933) | 1 |

* Licenses have not been issued.

# Book Notices

**Essentials of Medical Electricity.** By Elkin P. Cumberbatch, M.A., B.M., D.M.R.E., Medical Officer in Charge, Electrical Department, St. Bartholomew's Hospital, London. Eighth edition. Cloth. Price, $5. Pp. 528, with 162 illustrations. Cleveland, Ohio: Sherwood Press, 1939.

This posthumous volume presents the labors of a student of electrotherapeutics in England and offers a detailed exposition of the diverse indications and technics of electrical procedures in medical practice. The text proper reveals meticulous diction, erudition and authoritative mellowness that become fully substantiated on repeated reading. Cumberbatch's reputation for lucid and painstaking detail may be ascribed to his years of apprenticeship under Sir Lewis Jones, the distinguished pioneer whom he succeeded as ranking officer at St. Bartholomew's Hospital, in a service almost as ancient in electromedical tradition as this oldest of London institutions. His special services in the World War and his succeeding experiences in the subsequent years as instructor and examiner in electrotherapy gave him that further orientation which raised the succeeding editions of this contribution to the most authoritative level on the subject. It is therefore not surprising that the demands for this work have brought about an eighth edition with extensive revision and enlargement which includes a review of electrothermic methods and the mode of action of short wave diathermy. Throughout the twenty-seven chapters one observes that the author first attempts to establish a scientific basis for the many electrotherapeutic agents and methods utilized and then presents the clinical conditions for which they are best indicated. A good third of the book is devoted to the exposition of technical and biophysical problems related to its clinical application. It critically evaluates the electrochemical and physiologic action of the galvanic, faradic, sinusoidal and high frequency currents. Approximately another third is devoted to the application of the direct current to certain maladies by common ion transfer of drugs and the testing for reactions of muscles and nerves under normal and pathologic conditions. Finally, the author discusses the uses of medical and surgical high frequency current and the physical principles underlying the theory and practice of medical electricity. There are appended fifteen plates illustrating motor points of muscles and a workable index. The absence of a bibliography for collateral information demanded by students and critical readers is regrettable for a work that promises to become the classic in its field.

**A Doctor's Holiday in Iran.** By Rosalie Slaughter Morton, M.D. Foreword by Surgeon-General Hugh S. Cumming (Retired). Cloth. Price, $3. Pp. 335, with 20 illustrations. New York & London: Funk & Wagnalls Company, 1940.

A metamorphosis has been going on in Persia, now called Iran, since the present shah, Riza Pahlavi, came to the throne about fourteen years ago. The change that is taking place is comparable to the metamorphosis that has occurred in Turkey under the rule of Kemal Pasha. The present shah rose from the ranks and came into this high office after a highly successful and popular service in the army. He is as different from his predecessors as is the new age in Iran from the twenty-five centuries of its history that have preceded him. He has risen through ability from poverty. He has common sense, much intelligence, is democratic, and although a dictator is consistently working toward a democracy. The author decided to go to Persia to observe social changes. Her book is an account of what she observed in traveling about the country, associating with natives in their bazaars and homes. Being a physician, the author was especially interested in medicine. She visited the American Hospital in Teheran, the American Missionary Hospital in Tabriz and the Meshed Hospital near the Afghanistan border. Some of the patients observed are described. Superstition is still broadly extant in Iran. The use of blowing, spitting and stroking to heal the sick are common leftovers from ancient animism, some of which Mohammed incorporated into his teachings. Tiny shells and blue beads are considered especially effective in warding off evil. A charm is thought to be a greater benefit than reasonable care in the prevention of disease, and yet in the early days there was greater scientific knowledge in Arabia and Persia than anywhere else in the world. Wars in the sixteenth century retarded scientific progress, and the pharmacopeias of Persia reverted to the primitive. While Persian doctors centuries ago were among the most notable scholars, in the hands of their followers their teaching became involved with astrology, necromancy and omens and the practice of medicine degenerated into superstition. The author has caught much of the beauty in the art and culture of Iran. Her account will be especially appreciated by any one interested in history and travel.

**Sexual Disorders in the Male.** By Kenneth Walker, F.R.C.S., Surgeon to the Genito-Urinary Department, Royal Northern Hospital, London, and Eric B. Strauss, D.M., F.R.C.P., Physician for Psychological Medicine, St. Bartholomew's Hospital, London. With a foreword by Sir Walker Langdon-Brown, M.A., M.D., D.Sc. Cloth. Price, $3. Pp. 548. Baltimore: William Wood & Company, 1939.

This is a work by a urologist and a psychoanalyst. It is practical but unfortunately contains some glaring errors. The authors seem to be well acquainted with similar works by American authors, for they frequently quote from these works. Nevertheless they state in the introduction that "although there are several excellent reference books on sexology, notably those of Havelock Ellis, there exists no practical manual on how to deal with the various forms of sexual disability that are met with in the consulting room." Another statement which is hard to imagine emanating from a urologist is: "Mr. Kenneth Walker has become convinced by clinical experience that something like 90 per cent of sexual disorders in the male are mainly psychological in origin and that the success claimed for surgical procedures in such cases is chiefly due to their suggestive value." If such a statement had come from a psychoanalyst, one would not be surprised, but coming from a urologist and such a prominent and able urologist as Mr. Kenneth Walker it is hard to understand. The book gives much practical and useful information. It points out the importance of interviewing the wife in some cases of impotence. Although this has been emphasized in other works on sexual disorders, it cannot be too often repeated. The authors wisely state that the treatment of sexual inversion by psychoanalysis is unsatisfactory. The portion of the work describing the treatment of masturbation was evidently written by the psychoanalyst and is typical of psychoanalytic conception: "What calls for treatment here is the secondary anxiety arising out of the habit; and it is encouraging to realize that the abolition of this secondary anxiety involves the cure of the habit itself. The psychotherapeutic method of preference in such cases is reassurance, explanation and reeducation." Not one word is here said of the congestion in the prostate and the prostatic urethra. Experience in thousands of cases has shown that a relief of such congestion may cure the masturbator without any reference to the methods advocated.

**Infra-Red Irradiation.** By William Beaumont, M.B.C.S., L.R.C.P., Physician in Charge, Physiotherapy Department, Westminster Hospital, London. With a foreword by Lord Horder, K.C.V.O. Second edition. Fatherhold. Price, 6s. 6d. Pp. 159, with 20 illustrations. London: H. K. Lewis & Co., Ltd., 1939.

This small volume professes to be a critical study of that part of the spectrum which radiates a certain portion of energy sensed and interpreted as heat. Though the author appears to lean on a number of recognized monographs on this subject, he raises the implication that the present use of infra-red therapy still lacks a scientific basis, which by innuendo is to be established in his contribution. Unfortunately the text presents nothing strikingly new and in the main is a repetition of both authoritative data and moot problems culled from various sources. Considering that infra-red is in wide use, it is essential for any author on this method to present the fundamental biophysical and physiologic problems for the purpose of confirming by personal study such quoted opinions as are at variance with one another. As a result of such omission the exposition leaves the reader in the dilemma of accepting or rejecting diverse opinions expressed by individuals other than the author. The actual need for a truly scientific work so far as concerns debatable problems is their solution by laboratory research. This the author has failed to give, so that the book is reduced to the status of a primer. Although the work is now in its second edition, the diction leaves much to be desired nor is the text free from

certain factual errors. Thus Ampère is again stated to have been a Swedish physicist, when his French nationality is common knowledge. The book is divided into six chapters, the first two offering in abbreviated and elementary form the physical and physiologic fundamentals of infra-red radiation. The remainder is devoted to a description of popular apparatus, the technic and the treatment of some common symptoms and disorders, and concludes with a tabulation of the results of treatment in more than 1,000 cases. At the outset the author has taken the laudable attitude of warning against regarding this method as a panacea and of ascribing to it on the basis of his clinical experience the role of a useful adjuvant.

**Lee on the Lower: An Historical Novel. By Ralph Cannon. Cloth. Price, $2.50. Pp. 188. New York: Saravan House, 1940.**

Robert E. Lee as a young lieutenant in the engineering corps of the United States Army was ordered to St. Louis in 1837 to supervise work on the Mississippi River which would deepen the channel at St. Louis. During a part of this period of service, Lee's family and Dr. William Beaumont's family both lived in the mansion of Governor William Clark on the water front. The author has made a delightful story out of the association of these two famous families at that time, which gives a glimpse into the social life, the efficient and methodical ways in which Lieutenant Lee conducted his engineering work, and a brief account of the renowned physiologic experiments of Dr. Beaumont. The Canadian voyageur Alexis St. Martin is said to have lived with Dr. Beaumont and performed the duties of acting as servant at some of the social occasions described. The basis of the story is a collection of unpublished letters from the Lee family to the Beaumont family written after Lieutenant Lee had been ordered elsewhere. These letters were obtained for the author by Dr. Arno B. Luckhardt, professor of physiology at the University of Chicago, who obtained them for a museum display from Ethan Allen Beaumont of Green Bay, Wis., a grandson of Dr. Beaumont. Unfortunately the replies of the Beaumonts to the Lee letters have not been found. The author suggests that they may have been ransacked while the army was occupying Arlington, Lee's home in Virginia, just across the river from Washington, during the Civil War. The story serves also to show the admirable qualities in Lee as a young man, qualities of which the entire world learned later in Lee's life.

**Accepted Dental Remedies Containing a List of Official Drugs Selected to Promote a Rational Dental Materia Medica and Descriptions of Acceptable Nonofficial Articles 1939. Council on Dental Therapeutics. Cloth. Price, $1. Pp. 304. Chicago: American Dental Association, 1939.**

This valuable compendium is frankly modeled on New and Nonofficial Remedies and Useful Drugs of the Council on Pharmacy and Chemistry of the American Medical Association, which are, of course, much older than the dental publication. The book is in handy pocket size and is competently indexed. The products included are classified and grouped according to chemical composition or therapeutic use. At the head of each grouping appears a compendious general statement bringing out the characteristics of the preparations which are of interest and usefulness to the dentist. The same purpose is excellently carried out in the brief statement of actions and uses under each different drug. For example, under Calcium Compounds there is given a concise statement of present day knowledge on the use of calcium preparations as aids to proper calcification, possible prevention of caries, and the relationship of vitamin D and parathyroid. Under the various calcium compounds included appear terse indications for dental therapeutic use and technical specifications for those which may be used as abrasives in dentifrices. Under dentifrices are listed some fifty commercial brands of dental pastes, powders and creams. This is a marked increase over the number listed in former editions. It must be concluded therefore that the work of the Council on Dental Therapeutics is bearing fruit and that commercial houses in increasing numbers are making their preparations and claims in accordance with the council's rational and enlightened rules. It is to be hoped that the dental profession will continue increasingly to support the work of their council in this and other respects.

The book contains an excellent outline on symptoms and treatment of acute poisoning; useful tables of solubilities, weights and measures; a brief but comprehensive therapeutic index, with a suggestive and rather extensive set of formulas utilizing the drugs described in the book. A complete bibliographic index to reports on articles found unacceptable by the council completes a handbook that should be the vade mecum of every practicing dentist and dental student.

**Frontier Doctor. By Urling C. Coe, M.D. Cloth. Price, $2.50. Pp. 304. New York: Macmillan Company, 1939.**

A young medical graduate arrived in Bend, Oregon, in 1905 ready to begin practice in a new pioneer town a hundred miles from a railroad. He spent the night in a room shared with five other men and dressed next morning in freezing cold surrounded by a virgin pine forest which extended westward mile after mile to snow covered mountains. Here in the heart of the last pioneer stock country of the West the author remained for many years practicing among cowboys, sheepmen, Indians and other hardy folk. His book of experiences in this wide open town is an exciting tale, well written. He delivered babies, fought epidemics and treated those wounded in rough and tumble fights among Indians, horse thieves and rustlers. He pictures some of the personalities in this community. Finally for nine years he was associated here in practice with a schoolmate from a Chicago school. One may spend pleasantly an afternoon or evening reading this interesting story.

## Bureau of Legal Medicine and Legislation

### MEDICOLEGAL ABSTRACTS

**Malpractice: Liability of Hospital and Medical Staff for Nonunion of Fracture of Femur.**—The Security Benefit Association, an incorporated fraternal insurance association, maintained for the use of its members a hospital separately incorporated as the "Security Benefit Home and Hospital Association." The plaintiff, a 56 year old woman, a member of the fraternal association and entitled to hospital benefits, was admitted to the hospital in April 1933 for a series of operations including a cholecystectomy, the removal of bunions and resection of her coccyx. She was attended by Dr. Hiebert and other physicians, all of whom were employed by the hospital on a salary basis as resident physicians and not as independent practitioners. May 10, two days after the last operation, the patient fell out of bed and sustained a subcapital fracture through the neck of her left femur. Because her operative wounds had not yet healed, treatment of the fracture was complicated. The fracture was reduced and immobilization instituted by a particular type of plaster cast, variously described as a "well leg traction splint" or "Jones Modified Traction cast," apparently the Jones method of incorporating a screw traction apparatus in plaster boots enclosing both the injured and the well leg from the knees to the toes. She contracted boils and suffered great pain in her back in the region of the operative wound for the removal of her coccyx, which wound discharged pus. After taking check-up roentgenograms the plaster cast was removed by Dr. Hiebert on June 12, four weeks and five days after the reduction of the fracture. About seventy diathermy treatments were administered by one Musick, a hospital attendant who was neither a physician nor a nurse. Nonunion of the fracture resulted. The patient was discharged from the hospital Sept. 22, 1933. During the next five months she underwent treatments from a half dozen physicians, not connected with the hospital, designed to build up her strength. A Whitman's reconstruction operation was performed on her left hip in February 1934.

The patient brought suit for malpractice, Sept. 20, 1935, and recovered judgment against the fraternal association, the hospital and Dr. Hiebert on a finding of the jury that: (1) she had sustained injuries due to unskilful treatment or lack

of treatment during her hospital stay; (2) the hospital permitted activities not properly supervised which could not have maintained immobilization after the removal of the cast; and (3) Dr. Hiebert and other hospital employees, including Musick, were guilty of unskilful treatment or failure to render treatment. The defendants then appealed to the Supreme Court of Kansas.

In passing on the contentions of the plaintiff as to the various ways in which the treatment administered to her by the hospital and its servants departed from good practice, the Supreme Court considered the testimony of physician-witnesses before the trial court. Dr. Hiebert testified that in a fracture of the type suffered by the patient he usually kept the cast on for about three months but that in this case he removed the cast sooner because the patient was suffering from sciatic neuritis and had become psychopathic. After removing the cast, he stated, he stabilized the injured leg with pillows and treated the neuritis. Two medical expert witnesses called by the defendants, in answer to a hypothetical question which assumed that the plaintiff suffered from sciatica and that she would become insane if the cast were not removed, testified that Dr. Hiebert under the circumstances was justified in removing the cast. One of these witnesses stated that his opinion was not based altogether on the belief that the patient would lose her mind if the cast was not removed. A medical witness called by the patient, who believed that the cast should have been left on longer, admitted that in fractures of the neck of the femur complications unrelated to the fracture sometimes make it necessary to remove the apparatus for fixation earlier than would be done otherwise.

It was not negligence, said the Supreme Court, not to enclose the injured hip in a plaster cast. In view of the plaintiff's condition there was no evidence that the method of fixation utilized was not proper under the circumstances. There was no evidence to support a charge of the plaintiff that no treatment had been rendered for five weeks after her leg had been placed in the cast. Neither, in the opinion of the court, was there negligence in permitting Musick to administer diathermy treatments. According to the evidence he had studied books on diathermy, had taken special training and had administered at the hospital about 3,000 prior diathermy treatments without any known harm. In the judgment of the court the charges of negligence made by the patient failed also because they were not mentioned in and could not be implied from the findings of the jury. The court also held that the defendants were not negligent in continuing to administer diathermy treatments until Sept. 21, 1933, even though those treatments caused the plaintiff pain since it did not appear from the evidence that such treatments could have been administered without causing pain.

Further, the court could not agree with a contention of the patient that the defendants, on learning that union was not taking place, should have instituted other treatment to induce union instead of concealing from the patient her true condition and the urgency for other treatment. Neither, in the opinion of the court, was it shown that the defendants failed to treat the patient with that degree of care and skill prevalent among hospitals and physicians in that vicinity, nor that a proper degree of care and skill would have caused the fracture to unite within a short time. Medical testimony was in accord that failure to obtain bony union in fractures of the neck of the femur is common particularly in patients of the plaintiff's age, where failure is estimated as occurring in from 35 to 50 per cent of the cases. It was not shown that some treatment other than that which the patient received would have been proper or advisable. The evidence did show that because of her physical condition the patient was unable to undergo some other treatments commonly used to induce union when the original treatment has failed. The jury's finding that when the cast was removed the patient was not suffering from "any ailment other than the fracture of the femur and the previous operations" was not supported by the evidence. In fact, as already stated, treatments to build up her strength to undergo the Whitman's reconstruction operation were necessary. Furthermore, stated the court, "there was no evidence that it was unprofessional, negligent or wrongful in this case (or in any case) for a physician to conceal from his patient her condition."

The court did not agree with a contention of the patient that, since the fraternal association and the hospital knew or should have known that Dr. Hiebert and the other physicians who treated the plaintiff were incompetent, they were negligent in employing them. The evidence, said the court, showed that prior to employing these physicians the hospital through its officials made a favorable investigation of their qualifications. The court was also of the opinion that a finding of the jury to the effect that the patient had been discharged too soon from the hospital on Dr. Hiebert's orders was unwarranted, since the evidence showed that the patient was discharged from the hospital at her own request.

The court found it unnecessary to consider what is described as the sharply debatable contention of the hospital association that it was a charitable institution and therefore immune from liability. The question as to whether or not the defendant associations, corporations, were unlawfully engaged in the practice of medicine was not before the court.

For the reasons stated, the Supreme Court, in effect, instructed the trial court to enter judgment for the defendants.—*Blackburn v. Security Ben. Ass'n et al. (Kan.), 86 P. (2d) 536.*

## Society Proceedings

### COMING MEETINGS

American Medical Association, New York, June 10-14. Dr. Olin West, 535 N. Dearborn St., Chicago, Secretary.

American Association for the Surgery of Trauma, Atlantic City, N. J., June 7-8. Dr. Ralph G. Carothers, 409 Broadway, Cincinnati, Secretary.

American Association for Thoracic Surgery, Cleveland, June 6-8. Dr. Richard H. Meade, 2116 Pine St., Philadelphia, Secretary.

American Association of Genito-Urinary Surgeons, Skytop, Pa., June 20-22. Dr. Charles C. Higgins, 2020 East 93d St., Cleveland, Secretary.

American Broncho-Esophagological Association, New York, June 5. Dr. Paul Holinger, 1150 N. State St., Chicago, Secretary.

American College of Chest Physicians, New York, June 8-10. Dr. Robert B. Homan Jr., P. O. Box 1069, El Paso, Texas, Secretary.

American College of Radiology, New York, June 12. Mr. M. F. Cahal, 540 North Michigan Blvd., Chicago, Executive Secretary.

American Dermatological Association, Colorado Springs, Colo., May 30-June 1. Dr. Fred D. Weidman, 36 Hamilton Walk, Philadelphia, Secretary.

American Gastro-Enterological Association, Atlantic City, N. J., June 10-11. Dr. Albert F. R. Andresen, 88 Sixth Ave., Brooklyn, N. Y., Secretary.

American Gynecological Society, Quebec, Canada, June 17-19. Dr. Richard W. TeLinde, 11 East Chase St., Baltimore, Secretary.

American Heart Association, New York, June 7-8. Dr. Howard B. Sprague, 50 West 50th St., New York, Secretary.

American Laryngological Association, Rye, N. Y., May 27-29. Dr. C. J. Imperatori, 108 East 38th St., New York, Secretary.

American Laryngological, Rhinological and Otological Society, New York, June 6-8. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Medical Women's Association, New York, June 9-10. Dr. Elizabeth Parker, 1835 Eye St., Washington, D. C., Secretary.

American Neurological Association, Rye, N. Y., June 3-7. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Ophthalmological Society, Hot Springs, Va., June 3-5. Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn., Secretary.

American Otological Society, Rye, N. Y., May 30-31. Dr. Isidore Friesner, 36 East 73d St., New York, Secretary Pro-Tem.

American Physiotherapy Association, New York, June 23-28. Mrs. Eloise T. Landis, 2065 Adelbert Rd., Cleveland, Secretary.

American Proctologic Society, Richmond, Va., June 9-11. Dr. Curtice Rosser, 710 Medical Arts Bldg., Dallas, Texas, Secretary.

American Radium Society, New York, June 10-11. Dr. William E. Cotslow, 1407 South Hope St., Los Angeles, Secretary.

American Rheumatism Association, New York, June 10. Dr. Loring T. Swaim, 270 Marlborough St., Boston, Secretary.

American Society of Clinical Pathologists, New York, June 6-10. Dr. Alfred S. Giordano, 531 N. Main St., South Bend, Ind., Secretary.

American Therapeutic Society, New York, June 7-8. Dr. Oscar B. Hunter, 1835 Eye St. N.W., Washington, D. C., Secretary.

American Urological Association, Buffalo, N. Y., June 24-27. Dr. Clyde L. Deming, 789 Howard Ave., New Haven, Conn., Secretary.

Association for the Study of Internal Secretions, New York, June 10-11. Dr. E. Kost Shelton, 921 Westwood Blvd., Los Angeles, Secretary.

Maine Medical Association, Rangeley Lakes, June 23-25. Dr. F. R. Carter, 22 Arsenal St., Portland, Secretary.

Medical Library Association, Portland, Ore., June 25-27. Miss Anna C. Holt, 25 Shattuck St., Boston, Secretary.

Montana, Medical Association of, Bozeman, June 18-20. Dr. Thomas F. Walker, 206 Medical Arts Building, Great Falls, Secretary.

National Gastroenterological Association, New York, June 4-6. Dr. G. Randolph Manning, Room 319, 1819 Broadway, New York, Secretary.

National Tuberculosis Association, Cleveland, June 3-6. Dr. Charles J. Hatfield, 50 West 50th St., New York, Secretary.

New Jersey, Medical Society of, Atlantic City, June 4-6. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New Mexico Medical Society, Albuquerque, May 27-29. Dr. L. B. Cabaniss, 219 West Central Ave., Albuquerque, Secretary.

Pacific Northwest Medical Association, Spokane, Wash., June 26-29. Dr. C. W. Countryman, 407 Riverside Ave., Spokane, Wash., Secretary.

Rhode Island Medical Society, Providence, June 5-6. Dr. Guy W. Wells, 124 Waterman St., Providence, Secretary.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### American Journal of Public Health, New York

**30:219-324 (March) 1940**

Epidemiologic Studies of Tuberculosis. L. L. Lumsden, Nashville, Tenn., and W. P. Dearing, Montgomery, Ala.—p. 219.
Development of Tuberculosis in Controlled Environment. R. E. Plunkett, G. W. Weber, W. Siegal, Albany, N. Y., and Rose R. Donk, Newark, N. Y.—p. 229.
Food Value and Economics of Skim Milk. J. S. Abbott, Washington, D. C.—p. 237.
Application of Phosphatase Test to Butter. E. H. Parfitt, W. H. Brown, Lafayette, Ind., and G. W. Shadwick Jr., Chicago.—p. 240.
Microbiologic Content of Paper Board Used in Packaging of Foods. J. R. Sanborn, Geneva, N. Y.—p. 247.
Microbiology of Paper and Paper Board for Use in Food Industry. F. W. Tanner, Urbana, Ill.; E. Wheaton, Maywood, Ill., and C. O. Ball, New York.—p. 256.
Incidence of Rabies in Dogs and Rats as Determined by Survey. G. A. Denison, Birmingham, Ala., and C. N. Leach, Montgomery, Ala.—p. 267.
Educating Medical Students and Other Groups Concerned with Registration of Vital Statistics Data. I. C. Plummer, Columbus, Ohio.—p. 270.
Needle Puncture Method for Determination of Bacterial Contamination of Paraffined Milk Containers. C. S. Mudge and D. C. Peord, Davis, Calif.—p. 273.
Health Education of the Public. W. F. Higby, San Francisco.—p. 278.

### Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

**24:133-264 (March) 1940**

*Therapeutic Quartan Malaria in Therapy of Neurosyphilis Among Negroes. T. C. C. Fong, Washington, D. C.—p. 133.
Quartan Malaria in Treatment of Neurosyphilis. M. M. Kroll, Baltimore.—p. 148.
Granuloma Inguinale: Successful Use of Giemsa Stain to Demonstrate Typical Pathologic Findings. L. J. Alexander and A. G. Schoch, Dallas, Texas.—p. 180.
Laboratory Diagnosis of Gonococcic Infections. Anne Chittenden Pitts, Baltimore.—p. 184.
Spirocheticidal, Trypanocidal and Mechanism of Activity of Organic Arsenical Compounds in Vitro and in Vivo in Relation to Therapeutic Effectiveness. J. A. Kolmer, Clara C. Kast and Anna M. Rule, Philadelphia.—p. 201.
*Changes in Long Bones of Newborn Infants Following Administration of Bismuth During Pregnancy. J. Whitridge Jr., Baltimore.—p. 223.
Effect Produced on Newly Contracted Syphilis by Transfusion of Blood Taken from Patients Affected with Late Stages of Syphilis. M. S. Bragin, Alma Ata, Soviet Union.—p. 228.
Use of Sulfanilyl-Sulfanilamide (Disulon) in Treatment of Sulfanilamide-Resistant Gonorrhea in the Male. J. C. Alexander, Dallas, Texas; M. A. Forbes, San Antonio, Texas, and A. L. Holloman, Frederick, Okla.—p. 234.

**Quartan Malaria for Neurosyphilis Among Negroes.**—Fong presents the results of quartan malarial therapy among 436 Negro neurosyphilitic patients. It is generally accepted that Negroes are particularly immune to the organism of benign tertian malaria and therefore are refractive to this type of malarial therapy. A total of 229, or 53.2 per cent, of the 436 Negro patients responded successfully following malarial inoculation. This is a far greater response than that following tertian malaria, but it is considerably lower than the figures quoted by other authors. Of this number, 13.9 per cent were markedly improved by treatment, 33.1 per cent were improved and 52.8 per cent were unimproved. There were thirty-eight, or 12.2 per cent, deaths in the successfully inoculated group not directly attributable to malaria. Six deaths were due directly to therapeutic quartan malaria. There appeared to be no definite correlation between clinical and serologic improvement and vice versa, with the exception that the majority of patients clinically improved showed concomitant serologic improvement.

**Bismuth in Pregnancy and Bones of Infants.**—Whitridge reports the results of studies that were carried out with the purpose of determining whether or not bismuth compounds administered intramuscularly to twelve nonsyphilitic pregnant women would produce changes in the skeleton of the newborn similar to those observed in the long bones of infants of syphilitic mothers who had received preparations of bismuth intramuscularly during pregnancy. The twelve women received weekly injections of 1 cc. of bismuth salicylate in oil for not more than eight administrations. In other respects antepartum management was conducted as usual, and the pregnancies progressed uneventfully and without complicating factors. Seven women were delivered within one week, one within eight days and four within from twenty-four to thirty-six days after the last administration of the bismuth compound. Roentgenograms of their children were taken within the first week of life. The roentgenograms of nine infants showed definite changes near the ends of the long bones. These changes consisted of areas of increased transverse bands of density similar to those described by Caffey. In two instances no changes could be detected and in one any alterations from the normal were so slight as to be questionable. In the two cases in which the roentgenograms were considered normal, the mothers had received eight and seven injections of the metal, respectively, and delivery took place within one week of the last injection. In the one questionable instance the bismuth compound had been given eight times and delivery occurred three weeks after the last administration. Apparently some factor other than the mere quantity of metal administered is involved in producing these changes. Ten of the twelve infants were normal full-term children and were well when discharged from the hospital. One infant died on the second day of life following a difficult breech extraction and death was undoubtedly due to trauma. Postmortem x-ray examination of the skeleton showed well defined bands of increased density. At necropsy intracranial and intra-abdominal hemorrhages were discovered. Chemical tests for bismuth were negative when portions of bone from this infant were examined. A severe anemia developed shortly after the birth of the last infant. With repeated blood transfusions the child improved rapidly and was discharged two weeks later in good condition. The study supports Caffey's assumption that the changes in the long bones of infants of treated syphilitic mothers were produced by bismuth and not by healed syphilitic osteochondritis.

### Annals of Surgery, Philadelphia

**111:337-512 (March) 1940**

Role of Surgery in Management of Duodenal Ulcer. J. J. Westermann Jr., New York.—p. 338.
Chronic Duodenal Ulcer: Procedures as Determined by Operative Pathology. J. W. Hinton and R. L. Maier, New York.—p. 348.
*Problems in Surgical Treatment of Chronic Duodenal Ulcers. R. Lewisohn, New York.—p. 355.
Perforations of Gastrointestinal Tract. H. W. Meyer, New York.—p. 370.
Postappendical Abscess in Rectovesical Pouch: Transrectal Drainage. C. F. Vale, Detroit.—p. 396.
Present Status of Carcinoma of Gallbladder: Study of Thirty-Four Clinical Cases. C. R. Lam, Detroit.—p. 403.
Carcinoma of Gallbladder: Study of Seventy-Five Cases. Gemma M. Lichtenstein and W. Tannenbaum, Chicago.—p. 411.
Torsion of Wandering Spleen: Complicated by Diaphragmatic Hernia. J. V. Bohrer, New York.—p. 416.
Prevention of Peritoneal Adhesions with Heparin: Experimental Study. E. P. Lehman and F. Boys, Charlottesville, Va.—p. 427.
*Malaria Simulating Acute Surgical Diseases of Abdomen. R. A. Daniel Jr., Nashville, Tenn.—p. 436.
Calcified Constrictive Pericarditis. E. L. Eliason and R. B. Brown, Philadelphia.—p. 446.
Danger in Use of Local Infiltration Anesthesia in Operations on Malignant Tumors. W. T. Peyton, Minneapolis.—p. 453.
Follicular Lymphoblastoma. B. Sherwin and M. Spirtes, New York.—p. 459.
Treatment of Compound Fractures of Long Bones. J. H. Heyl, New York.—p. 470.
Control of Air-Borne Bacteria in Operating Rooms and Hospital Wards: Preliminary Report. Elizabeth Chant Robertson and M. Elizabeth Doyle, Toronto.—p. 491.

**Surgical Treatment of Duodenal Ulcers.**—According to Lewisohn, partial gastrectomy with removal of the ulcer is the operation of choice for duodenal ulcer. Opposition to gastric resection persists because of technical difficulties inherent in the operative technic. He believes that, if gastric resection was technically as simple as a gastro-enterostomy or a pyloroplasty, every surgeon would employ it. Exaggerated statements have been made about the inherent mortality and the magnitude of the operative procedure in gastric resection. With some experience and with proper organization, the mortality in primary cases

of gastroduodenal ulcers should not be higher than about 5 per cent. The mortality following a subtotal gastrectomy for gastric ulcers is usually higher than that following partial gastrectomy for duodenal ulcers. Yet gastric resection for gastric ulcers is considered by most surgeons as a justifiable procedure, whereas gastric resection for duodenal ulcers is considered too radical. It appears that opposition to the procedure is due to some extent to the abuse of the term "subtotal gastrectomy." The term implies that only a small stump of stomach is left. This term is fitting for the operation for high gastric ulcers. When one is dealing with duodenal or prepyloric ulcers the removed part represents a little more than one half of the stomach. Partial, rather than subtotal, gastrectomy is the correct term for this operation. The term "gastric resection" is also incorrectly applied to certain operative procedures. The surgeon should distinguish between a prepyloric or a postpyloric Finsterer operation. The Finsterer operation puts the ulcer at complete rest and reduces the preoperative hyperacidity considerably. Thus the method has a sound principle. The same cannot be said of the palliative resection of Madlener. If temporary cures follow this method, they probably occur independently of the operation, not because of it. Perforation and hemorrhage, the serious complications of duodenal ulcer, have been more frequent in recent years because duodenal ulcer is still considered a medical disease, even after repeated medical failures. The fact that a fair percentage of ulcer cases are refractory to medical treatment must be recognized. The economic factor may at times place the ulcer patient in the surgical group. While partial gastrectomy is far superior to gastro-enterostomy or pyloroplastic operations, it is not a definite safeguard against a recurrence. The ideal method for permanent cure of chronic duodenal ulcer still has to be found and it is possible that it will be along medical lines. At present when a series of medical treatments have failed, partial gastrectomy is the best method. It relieves the patient of many years of suffering, safeguards him against the serious complications of perforation or hemorrhage and effects a permanent cure in about 90 per cent of cases.

**Malaria Simulating Acute Surgical Diseases of Abdomen.**—Daniel discusses the confusing picture produced by abdominal pain, which may be a manifestation of malaria. Surgeons are familiar with the postoperative fever caused by the lighting up of a chronic malarial infection. These cases sometimes occur in temperate regions. Daniel reports nine cases of malaria simulating acute abdominal disease. Eight of the patients were encountered in a total of 266 patients with malaria admitted to the Vanderbilt University Hospital during the last thirteen years. An analysis of the cases reveals that the diagnosis of malaria was suspected and established in six cases because of the presence of leukopenia on admission. A rise in temperature was accompanied by a leukopenia, sometime after admission, in three cases. Two patients had an unexplained chill and the parasites were found in the routine blood smear. Sudden onset of severe abdominal pain occurred in six cases, and in three the pain was at first relatively mild and gradually increased in severity. Nausea was present in all cases and vomiting in eight. Only three patients had prodromal symptoms, headache and general malaise, and only three gave a history of previous attacks of similar abdominal pain. The past history of two patients was of significance in suggesting malaria as a cause of the symptoms. Chills occurred during the present illness in only three cases. The spleen of only one patient was felt, and he presented such marked abdominal tenderness and muscle spasm that neither the liver nor the spleen could be palpated until several hours after the parasites had been found and quinine was administered. The liver of only one patient could be felt. Three of the patients had a definite involuntary rigidity of the abdominal wall at the time of admission. The two patients who gave past histories of malaria had received inadequate treatment. The other patients had never had symptoms of malaria and had not received antimalarial treatment. The importance of painstaking, unhurried examination of the blood in similar cases is emphasized. Parasites are often found by the thick drop method when they are not numerous enough to be seen in smears. Repeated examinations of the blood were performed in five cases before parasites were seen. Plasmodium vivax was found in the blood of seven and Plasmodium falciparum in the blood of two patients. The usual criteria for differentiation of malaria from the common, acute surgical diseases of the abdomen were strikingly inadequate in most of the nine cases. Leukopenia was present in eight. It may be of considerable aid in suggesting the presence of malaria. The examination of a blood smear and of thick drop led to the correct diagnosis in five. The finding of malarial parasites in the blood of patients who present characteristic signs of intraperitoneal disease does not exclude the possibility that such a disease may also be present.

## Archives of Surgery, Chicago

40:585-820 (April) 1940

Tumors of Lateral Thyroid Component. L. C. Cohn and G. A. Stewart, Baltimore.—p. 585.
*Relation of Tumors of Lateral Aberrant Thyroid Tissue to Malignant Disease of Thyroid Gland. R. Ward, San Francisco.—p. 606.
*Plasmocytoma of Thyroid Gland: Report of Case. R. C. Shaw and F. B. Smith, Preston, England.—p. 646.
New Method of Ureteroileostomy Utilizing Peritoneum. R. E. Brackin, Kenilworth, Ill.—p. 658.
Metastasis of Carcinoma to Scalp: Distinction from Cylindroma and from Carcinoma of Dermal Appendages. H. Montgomery and R. R. Kierland, Rochester, Minn.—p. 672.
Clinical Classification of Lesions of Lower Extremities Associated with Diabetes: Guide for Operation and Level of Amputation. F. W. Williams and T. J. O'Kane, New York.—p. 685.
Persistence of Meckel's Diverticulum: Report of Case. C. B. Rentschler, Reading, Pa.—p. 694.
Effects of Pressure on Tissues. B. Brooks and G. W. Duncan, Nashville, Tenn.—p. 696.
Changes in Plasma Volume Due to Decompression of Distended Small Intestine. J. Fine, F. Fuchs, Boston, and S. Gendel, Los Angeles.—p. 710.
Gastric Secretion: I. New Gastric Pouch with Nonleaking Stoma and Intact Nerve Supply: Description of Two Stage Technic Used on Dog. O. Cope, C. E. MacMahon, A. Hagströmer and R. H. Thompson, Boston.—p. 717.
*Hyperplasias of Mammary Gland in Human Being and in Mouse: Morphologic and Etiologic Contrasts. H. C. Taylor Jr. and C. A. Waltman, New York.—p. 733.

**Tumors of Lateral Aberrant Thyroid and Malignant Tumors of Thyroid.**—According to Ward, the dividing line between benign and malignant tumors is nowhere less sharply drawn than in tumors of thyroid tissue showing papillary design. Fifteen cases of tumors of aberrant thyroid tissue found in the pathologic material of 4,274 operations are presented in detail. There were ninety-five malignant tumors in normally situated thyroids. Twelve of the growths of the aberrant thyroid were tentatively considered by the author as malignant and three as benign. Of three patients dead of lateral tumors, two had growths of the papillary type and one a malignant adenoma. Of the twelve malignant tumors, seven were either predominantly papillary or showed some characteristics of that growth, while five showed no tendency toward papilliferous change. The most common location of lateral aberrant tumors is along the course of the sternocleidomastoid muscles. The tumors were single in only three instances. The remaining twelve cases were instances of multiple tumors, forty-two located in the left side of the neck and twenty-nine in the right. In three cases there was no associated involvement of the thyroid. In papillary tumors a papillary tumor was considered malignant in the presence of microscopic evidence of invasion of the capsule, blood vessels or lymph nodes. Regional or distant metastases were considered gross evidence of malignant change. Multiple lateral tumors, whether accompanied by similar tumors in the thyroid or not, do not constitute evidence of malignant change by themselves, and the presence of lymphoid elements in lateral tumors does not necessarily indicate that they are metastases to lymph nodes. Many of the changes which would bespeak a malignant condition in other organs are seen in the thyroid as a response to stimulation of the gland to greater activity. There is little evidence that the change from a benign to a malignant tumor of papillary structure is not a reversible process. There is considerable difference of opinion as to the origin of lateral aberrant thyroid nodules. If lateral aberrant thyroid tissue develops from embryonal rests, as was suggested by Wegelin, its response to stimulation may be the formation of papillary growths. If the factors causing stimulation are removed or altered, the tumors may regress unless they have reached an irreversible stage or the individual biologic factor resistant to cancer in the host is lacking. The loss of this assumed factor may explain the progression to a malignant

growth in older persons, and the retention of it may account for the apparently benign course of many of these tumors in children. Dunhill has reported complete disappearance of recurrent lateral tumors in two children on administration of large doses of thyroid substance. However, in adults the danger that an irreversible change will take place or has already taken place is too great to warrant less than complete removal of all lateral tumors and, contrary to the opinion of Crile, the application of radiation as a postoperative measure. It may be worth while to administer thyroid substance to all adult patients with such tumors, especially to those showing a thyroid deficiency. The author points out that the statistical comparison of malignant tumors of lateral aberrant thyroid tissue with those arising in the thyroid proper shows that the former are found in a younger age group, that they are more equally distributed between the sexes and that the mortality rate is less than half as great. Despite the more favorable mortality rate, the ratio of recurrence is high. Only four of the fifteen patients have remained free from the disease after a single operative removal. There were two deaths from papillary tumors, one from pulmonary metastases and one the author believes was caused by metastases from a lateral nonpapillary tumor. In view of this he feels that a guarded prognosis should be given in similar cases and that more deaths will be found in the cases reported by other investigators if a sufficiently long period of observation is maintained.

**Plasmocytoma of Thyroid.**—Shaw and Smith report what they believe to be the first case of plasmocytoma arising in the thyroid. The tumor appears to be related to Riedel's chronic thyroiditis. The case is that of a childless married woman aged 50 presenting a swelling in the region of the thyroid. The swelling slowly increased in size. The patient's only complaint was a sensation of choking when she lay in bed with her neck extended. The swelling conformed in outline to the shape of the thyroid and was free from the overlying skin, which was slightly reddened and edematous, and from the sternocleidomastoid muscles. No abnormality but osteo-arthritis of the knees and shoulders since the age of 36 was found. The basal metabolic rate was within normal limits. A total thyroidectomy was performed. The neck presented a normal appearance eighteen months later. A maintenance dose of thyroid substance has been given daily. Clinical, macroscopic and microscopic study of the tumor revealed dominance of the plasma cell and the relative paucity of lymphadenoid tissue, and the macroscopic appearance and clinical history resembled that observed in cases of Riedel's chronic thyroiditis. Microscopically the growth was an almost perfect example of a plasma cell tumor. The one point of distinction between this case and cases of thyroiditis was the exceptional prominence of the plasma cell. There is a division of opinion as to whether these tumors are inflammatory or true neoplasms. The association in their case with the changes known as chronic thyroiditis suggests that lesions occurring diffusely in the neck and those arising as localized masses in the nasopharyngeal mucosa (and more rarely in other places) have a common cause. In all the reported cases of thyroiditis, syphilis and tuberculous infection were excluded, nor could pyogenic organisms be held responsible. There must obviously be other etiologic factors which initiate a stimulus resulting in destruction of the thyroid in an otherwise healthy person, or the growth of masses of tissue in the neck. The authors believe that their case affords a clue in the long-standing osteo-articular and periarticular trophic disturbances. The importance of the adrenal hormone in connection with the conductivity of the neural impulse in the sympathetic system suggests that there is an intricate and delicate mechanism by which the passage of physical stimuli between the central nervous system and the thyroid or other tissue is intimately associated with the endocrine secretions. They consider the changes occurring in their case as one aspect of the pathologic course of a condition which is itself uncommon, namely Riedel's chronic thyroiditis, and that these conditions are expressions of tissue cell hyperplasia following a physiochemical disturbance that may be dependent on a complex cycle of causes in part due to disturbance of the neural control and in part of endocrine origin. They conclude that the plasmocytoma in this case belongs to a type of plasma cell hyperplasia which may occur in conjunction with lymphocytic hyperplasia, the two cellular elements varying in different cases. In some the plasma cell predominates, in others the lymphocyte, and in still others the two are present in more or less equal proportions. The ultimate course of such a hyperplasia appears to be governed either by local tissue reaction or by cessation of the initial stimuli. They conclude tentatively that these uncommon changes are due to an imbalance of the neuro-endocrine control of the tissue cells. Disturbance of the neural impulse or of the physiochemical mechanism results in abnormal stimuli productive of intensive proliferation of the connective tissue cells and hyperplasia and destruction of normal glandular elements. Plasmocytoma of the thyroid, chronic thyroiditis and other extramedullary plasmocytomas are all expressions of a common pathologic process.

**Hyperplasias of Mammary Glands.**—The study is concerned with contrasting the morphologic structure of supposedly precancerous lesions in the mouse and in man and with the endocrine disturbances underlying each. The phases of the problem investigated by Taylor and Waltman were (1) microscopic characteristics of the two major lesions of chronic mastitis (adenofibrosis and hyperplasia of the ducts), (2) clinical evidence of ovarian dysfunction in women with chronic mastitis, (3) gross and microscopic structure of the mammary glands of two strains of mice differing in their susceptibility to mammary cancer, (4) a search for evidence of a specific physiologic endocrine difference between the two strains and (5) a study of the mammary glands of mice after injection of various endocrine substances. The pathologic material consisted of mammary tissue removed at operation from 103 patients with chronic cystic mastitis. Clinical aspects of the disease of the breast and data on the reproductive and menstrual histories were available. The lesions were subdivided into four groups: distortion of the mammary architecture owing to hyperplasia of fibrous tissue or of normally formed acini (adenofibrosis), proliferation of atypical acini (adenosis) and inflammatory or neoplastic disease of the ducts. The acinar proliferation is the form of human mammary lesion most closely resembling abnormal proliferation developing in the glands of mice susceptible to mammary carcinoma. There are at least two separate entities which have been called chronic cystic mastitis. The first is characterized by a diffuse nodularity and by premenstrual pain. The basic microscopic lesion is fibrosis or adenofibrosis involving the interstitial fat and the periacinar tissue. The ducts are but slightly affected. The condition is analogous to adenomyosis of the uterus and should be termed adenofibrosis. The second type is characterized by a discharge from the nipple, often associated with palpable dilatation of the ducts near the areola. The microscopic alterations are edema of the lobules, dilatation of the ducts, periductal inflammation and possibly some hyperplasia of the lining of the ducts. The disease should be termed nonpuerperal lactation, periductal inflammation or duct hyperplasia. A third type is perhaps to be recognized in more or less local lesions, such as a single papilloma in the larger ducts or the isolated nodules of Schimmelbusch's disease. The clinical evidence of ovarian disorder obtained from the microscopic study showed that of forty-seven patients with painful nodular breasts only seventeen had borne children, while of forty-six patients with discharge from the nipple forty-one had children. All the patients with a simple milky discharge had been pregnant. This supports the claim that two distinct entities are being dealt with. Disturbances of the menses affect a minority of patients with chronic mastitis but are more frequent than in normal women. A decrease in the amount and duration of the menstrual flow in cases of painful nodular breast (adenofibrosis) was again evident in about a fifth of the cases. The consistency with which this rather uncommon anomaly of menstruation has been reported in this type appears to establish its association with the disease. Delay in menstruation may be present. Papillomas of the ducts and circumscribed adenomatous proliferations are to be regarded as nearly independent neoplasms, while the more diffuse processes, occurring before the menopause, are to a greater extent dependent on ovarian function. The significance of endocrine abnormalities in chronic mastitis assumes importance from the observation of mice susceptible to mammary carcinoma. Striking differences were observed in the spontaneous lesions resembling chronic mastitis in two strains of mice as early as the third month of life. The essen-

tial difference was a vast increase in the number of acini in the cancer susceptible strain. The mammary glands of these two strains are similar at birth. The hereditary factor is probably not in the gland but in stimuli which make themselves evident in morphologic change in the mammary gland early in the life of the animal. The early changes which eventually lead to spontaneous carcinoma in mice affect essentially the peripheral portions of the mammary gland. The more common characteristics of so-called chronic cystic mastitis were not observed to occur spontaneously in mice. The strain with excessive mammary proliferation had a much larger ovary with many more corpora lutea than the cancer resistant strain. Less striking differences were present in the adrenal and the thyroid. No differences in the anterior lobe of the pituitary were observed. However, the strains studied are not necessarily representative of all cancer susceptible or cancer resistant groups. The differences in the ovaries of the two strains indicate the need of morphologic examination of the ovaries of women with hyperplastic and neoplastic disease of the breast. The authors studied the effects of an excess of four different endocrine principles on the two strains. The basic difference, diffuse adenomatous proliferation of acini, was persistent no matter what endocrine principle was injected. Morphologically similar structures are sometimes seen in human mammary disease, but their presence does not constitute an essential feature of "chronic mastitis." The diffuse fibrosis or adenofibrosis, the most common form of benign mammary disease in women, has no morphologic counterpart in the mammary lesions of mice, whether spontaneous or induced by endocrine substances. Retained secretion in dilated ducts, moderate hyperplasia of the lining of the ducts and signs of periductal inflammation are closely imitated by lesions in mice which develop after prolonged administration of endocrine substances, especially estradiol. Complex neoplastic lesions occurring in the human breast, such as papillomas or proliferation of the epithelium, do not develop in the breast of the mouse either spontaneously or after prolonged administration of estrogens.

## Georgia Medical Association Journal, Atlanta

**29:89-204 (March) 1940. Partial Index**

Plantation Medicine. V. H. Bassett, Savannah.—p. 112.
Pages from the History of the Georgia Medical Society of Savannah, Georgia: Second Oldest Active City Medical Society in the United States. V. H. Bassett, Savannah.—p. 122.
Two Physicians and Two Periods, in the Medical History of Georgia: Dr. Joshua Elder White of Savannah and Dr. Alexander Jones of Lexington. V. H. Bassett, Savannah.—p. 137.
The Medical Career of John LeConte, 1818-1891, Who Was a Physician in Savannah from 1842-1846, with Discussion of Status of Medical Practice at That Time. V. H. Bassett, Savannah.—p. 149.

## Journal of Urology, Baltimore

**43:427-532 (March) 1940**

*Hypertension Associated with Unilateral Nephropathy. R. M. Nesbit and R. K. Ratliff, Ann Arbor, Mich.—p. 427.
Horseshoe Kidney Lying Between Great Vessels: Case. J. R. Meek and G. H. Wadsworth, Detroit.—p. 448.
Histogenesis and Physiology of Renal Glomerulus in Early Postnatal Life: Histologic Examinations. P. Grunwald and H. Popper, Chicago.—p. 452.
Infarction of Prostate and Volumetric Changes Produced by Lesion: Report of Three Cases. J. W. Hubly and G. J. Thompson, Rochester, Minn.—p. 459.
*Urologic Manifestations of Appendicitis. C. D. Ehlert, Alton, Ill.—p. 468.
Intestinal Phase in Urologic Disease: III. Role of Colon in Urolithiasis. R. Turell, New York.—p. 476.
Rubin Ureteral Calculus Clamp. J. S. Rubin, Los Angeles.—p. 481.
Sulfanilyl-Sulfanilamide (Disulon) versus Sulfanilamide in Treatment of Acute Gonorrhea in the Male. L. J. Roth, Columbus, Ohio.—p. 483.
Comparative in Vitro Action of Sulfanilamide, Sulfapyridine and Sulfathiazole in Urine. Justina H. Hill, Baltimore.—p. 491.
Cystometric Observations in Asymptomatic Neurosyphilis: II. E. L. Brodie, I. Helfert and I. A. Phifer, Buffalo.—p. 496.
Rupture of Urinary Bladder. H. Culver and W. J. Baker, Chicago.—p. 511.

**Hypertension and Unilateral Nephropathy.**—Nesbit and Ratliff report nine cases of hypertension associated with chronic inflammatory nephropathy, three cases of chronic inflammatory nephropathy without hypertension, two cases of hypertension associated with obstructive nephropathy and one case of hypertension associated with sclerotic and cystic nephropathy (ischemic) resulting from trauma. Experimental and clinical investigations have established a relationship between nonnephritic renal lesions and hypertension. Numerous cases of hypertension have been reported associated with unilateral and bilateral chronic sclerosing pyelonephritis. Vascular changes within the infected kidney associated with hypertension have been reported by most observers. That the same vascular changes may occur in chronically infected kidneys without associated hypertension seems evident from cases presented. Nephrectomy appears to be a justifiable procedure in cases of unilateral pyelonephritis with associated hypertension. Improvement may be expected in this group provided the functioning capacity of the remaining kidney is unimpaired. Secondary vascular changes elsewhere in the body may militate against recovery. The authors point out that the results of treatment in their two cases of obstructive nephropathy with hypertension clearly demonstrate that the causal relationship between obstruction and hypertension is not due to renal insufficiency. They suggest a reflex rather than a toxic or humoral factor, since nephrostomy was as effective as nephrectomy in returning the blood pressures to a normal level. The one case of malignant hypertension occurred ten years after traumatic injury to the kidney. The possibility of a causal relationship between ischemic changes in this kidney and the hypertension suggests the advisability of periodic blood pressure determinations in all cases following traumatic injury of the kidney. The development of hypertension in such circumstances would appear to make prompt nephrectomy a rational procedure.

**Urologic Manifestations of Appendicitis.**—Ehlert reviews subjective and objective manifestations of appendicitis that might be confused with those of the urogenital tract, in particular the lower urinary tract. The opposite situation is not infrequent. He classifies urologic manifestations of appendicitis as follows: (1) disorders of micturition (frequency of urination, pain on urination, dysuria and retention of urine), (2) abnormalities of the urine (hematuria, pyuria, albuminuria and anuria), (3) pain in the right testis or retraction of the testis, (4) renal or ureteral colic and (5) tenderness in the right costovertebral angle. If disorders of urination were due to sympathetic irritation, as Deaver suggests, one would expect to find them associated with negative urinary changes, but such is rarely the case. In the presence of symptoms there are usually found varying amounts of blood, pus or casts, along with micro-organisms, in the urinary sediment. Such observations are much more compatible with the theory of intimate contact of the appendix or the inflamed peritoneum with some part of the urinary tract. Operative and postmortem observations demonstrated that this is the usual occurrence. The site most frequently involved is the right ureteral wall at the brim of the bony pelvis. In place of "toxic hematuria," "reflex renal congestion" and similar concepts, one may find a more logical and more easily verified solution in the frequently found intimate association of the inflamed appendix with the right ureteral wall. Pyuria, both slight and massive, not infrequently encountered in appendicitis, may be similarly explained. An inflamed appendix in actual contact with the right ureteral wall produces a periureteritis and ureteritis that result in pus cells passing into the ureteral lumen and eventually appearing in the urine. An actual pyelitis depending on a lymphogenic ascent of colon bacilli up the periureteral lymphatics to the kidney may, and in all probability does, play some part. In an analysis of 300 cases of pyelitis, Van Duzen listed appendicitis as being the probable etiologic factor in 7.6 per cent. Massive pyuria may be seen following the rupture of an appendical abscess into the bladder. Albuminuria seen in appendicitis may usually be accounted for by the pus and blood cells present in the urine at the same time. Anuria is a rare accompaniment. According to Cope, testicular pain occurs in about 5 per cent of the cases of appendicitis. It may precede the abdominal pain by an hour or two. Pain resembling renal or ureteral colic is frequently seen when the appendix or its inflammatory exudate is in contact with the renal pelvis or the right ureter. Tenderness in the right costovertebral angle is seen in many cases of appendicitis, particularly in those in which the appendix occupies a retrocecal position.

## New England Journal of Medicine, Boston

**223:425-470 (March 14) 1940**

Surgery of Stomach and Duodenum: Medical Aspects. C. M. Jones, Boston.—p. 425.
*Id.: Gastroscopic Examination. E. B. Benedict, Boston.—p. 427.
Id.: Surgery of Stomach. A. W. Allen, Boston.—p. 434.
Id.: Surgery of Duodenum. F. H. Lahey, Boston.—p. 444.
Psychiatry. V. P. Williams, Boston.—p. 452.

**Gastroscopic Examination.**—The concept of gastric disease has undergone considerable change since the introduction of the Wolf-Schindler flexible gastroscope. It is now possible to see the inside of the stomach and to observe changes in the gastric mucosa not demonstrable by any other method. Benedict discusses the use of the gastroscope in the various gastric disorders and cites illustrative case histories. On the basis of observations extending over a period of six years, he concludes that gastroscopy is a safe procedure, easily performed and well tolerated by most patients, and that the information obtained is of great value to the surgeon. Since gastritis is the commonest disease of the stomach and since massive hemorrhage may come from gastritis alone, all patients with unexplained gastrointestinal bleeding should have a gastroscopic examination. Gastritis which frequently accompanies gastric or duodenal ulcer must be recognized and localized, particularly if surgical intervention is being considered. Since postoperative gastritis is a definite entity best recognized by gastroscopy, gastroscopic examination should always precede secondary intervention. In both gastric and duodenal ulcers the associated gastritis, which may seriously modify the medical or surgical management of the patient, is best studied by gastroscopy. Gastric ulcers not previously suspected have been demonstrated by the method. The gross appearance of the lesion, whether clean and sharply defined, as in benign ulcer, or dirty and irregular, as in malignant ulcer, and its response to treatment are points of great importance that should be studied by gastroscopy. The method is of value in the diagnosis of carcinoma in determining its location and extent and in differentiating benign and malignant lesions.

## New York State Journal of Medicine, New York

**40:311-384 (March 1) 1940**

*Sulfanilamide in Treatment of Scarlet Fever: Need for Research Point of View. A. C. Silverman, Syracuse.—p. 317.
Tuberculosis in Student Nurses. L. Brahdy, New York.—p. 326.
Spasmogenic Tendency and Its Relation to Eyes. R. K. Lambert, New York.—p. 334.
Camp Sanitation. C. A. Holmquist, Albany.—p. 341.
Use of Sulfanilamide in Treatment of Hemolytic Streptococcus Empyema. L. J. Leahy, Buffalo.—p. 347.
Distinctive Odor in Patients Receiving Sulfanilamide. S. Leibowitz, New York.—p. 363.
The Function of a Child Guidance Clinic. H. A. Steckel, Syracuse.—p. 364.
Relation of Food to Nonspecific Ulcerative Colitis. M. L. Bodkin, Brooklyn.—p. 368.

**40:385-460 (March 15) 1940**

Treatment of X-Ray Burns and Other Superficial Disfigurements. A. B. Cannon, New York.—p. 391.
Chronic Pyelonephritis: Cause of Hypertension and Renal Insufficiency. W. S. McCann, Rochester.—p. 400.
Prognosis of Nephritis and Nephrosis in Childhood. H. Schwarz, J. L. Kohn and S. B. Weiner, New York.—p. 409.
Friedreich's Ataxia Associated with Diabetes Mellitus. N. S. Schlesinger, Philadelphia, and K. Goldstein, New York.—p. 413.
Mechanical Obstructions of Small Intestine. W. F. MacFee, New York.—p. 424.
Trauma in Relation to Pulmonary Tuberculosis. C. E. Hamilton, Brooklyn.—p. 435.
Nutritional Study: Analysis of 100 Medical Admissions to St. Luke's Hospital. J. R. Scott and Margaret McAllister Janeway, New York.—p. 440.
Applications of Electro-Encephalography in the Practice of Medicine. H. Strauss, New York.—p. 444.

**Sulfanilamide for Scarlet Fever.**—According to Silverman, there has been a striking change in the character of scarlet fever over the last seventy-five years, the mortality in 1938 being but one one-hundredth of that in 1861, which was 100 per hundred thousand. This increasing mildness caused some difficulty in evaluating the therapeutic effects of serum and of sulfanilamide. The latter exerts no evident influence on the toxic phase of scarlet fever. The author refers to several studies which suggest that sulfanilamide may lessen the incidence of suppurative ear complications. No series large enough to be accepted as conclusive were published. As a basis for statistical consideration he analyzes a nonepidemic series of eighty-four cases admitted to the Syracuse City Hospital last year; forty-three patients were given sulfanilamide and forty-one served as controls and were given serum. A smaller ratio of suppurative otitis media was encountered in the sulfanilamide group. Of twenty-three toxic patients on admission given sulfanilamide suppurative ear conditions developed in two as compared to seven of nineteen similar control cases. Nevertheless definite conclusions are unwarranted on the basis of a small series. Sulfanilamide does not replace antistreptococcus serum in cases of toxemia. In severe cases with toxic and septic phases, combined treatment is indicated. For the sick patient it is justifiable, under proper safeguards, to incur the risk of serum reaction or drug intolerance.

## Radiology, Syracuse, N. Y.

**34:261-390 (March) 1940. Partial Index**

Antepartum Roentgenographic Diagnosis of Fetus Papyraceus. A. C. Johnston, Berlin, N. H., and M. C. Sosman, Boston.—p. 261.
Roentgenologic Aspects of Bronchomycosis. H. P. Doub, Detroit.—p. 267.
Differential Diagnosis of Nonspecific Interstitial Pneumonitis. F. J. Hodges, Ann Arbor, Mich.—p. 276.
*Miniature X-Ray Chest Film. H. E. Potter, Chicago; B. H. Douglas and C. C. Birkelo, Detroit.—p. 283.
*Roentgenographic Prognosis of Pulmonary Tuberculosis. J. Gershon-Cohen and J. T. Farrell Jr., Philadelphia.—p. 292.
Evaluation of Roentgen Therapy in Sinus Disease. J. R. Maxfield Jr. and C. L. Martin, Dallas, Texas.—p. 300.
Pulmonary Involvement in Lymphoblastomas, Special Reference to Roentgen Aspects. A. Hartung, Chicago.—p. 311.
Incidence and Significance of Apical Lesions in Pulmonary Tuberculosis: Pathologic and Roentgenologic Study. E. A. Addington and B. R. Kirklin, Rochester, Minn.—p. 327.
Benign Duodenocolic Fistula: Report of Two Cases. C. N. McPeak, Fitchburg, Mass.—p. 343.

**Miniature Chest Films.**—Potter and his co-workers find that a 4 by 5 inch film reproduction of a fluoroscopic image is small enough to constitute real economy and yet large enough to be readily interpreted without enlargement. The technic of producing this film comprises a modern x-ray installation with rotating anode tube capable of handling 400 milliamperes of current at from 60 to 80 kilovolts, an impulse timer and a tube-screen distance of 50 inches (125 cm.). The time necessary for exposure depends on the thickness of the chest and varies from one twentieth to four twentieths of a second. The fluorescent screen used is nearly seven times as fast as the usual Patterson screen. The lens has a rating of 1.5. This lens is capable of producing a sharp image in an area of 3 1/10 inches in diameter on the 4 by 5 inch film. For the best results the patient's chest image must be centered within this area. To test the capacity of this film 1,610 patients were examined with both the regular 14 by 17 inch film and the miniature film, taken at the same time. The readings were interpreted and recorded independently. A total of 271 patients were found to have various types of active tuberculosis. Five of the minimal lesions were missed in the interpretation of the miniature films. Two other minimal lesions were called "healed primary." All these lesions were small and might easily have been missed in a regular film taken at a different angle, a slightly different depth of breathing or with less perfect technic. In nearly every instance these missed lesions were superimposed over rib shadows. This constituted an error of 2.6 per cent. There were five small lesions of active primary infection or enlargement of the lymph nodes. None of these were missed in the miniature film. Of fifty-four dry pleurisies nine were missed, an error of 17 per cent. This unnecessarily large error was due to too much attention being given the apexes with the consequent throwing out of focus of the bases. This has since been balanced so that the bases are nearly as well demonstrated as the apexes, with the result that this error can be decreased with a little extra care. From the regular films twenty-eight cases were classified as "minimal healed tuberculosis." Eight of these were not considered sufficiently significant in the miniature film to be mentioned. If a descriptive report had been given, it is likely that no significant error would have resulted. Two of twelve cases of valvular cardiac lesions from which symptoms resulted similar to those found in tuberculosis were called mixed but, when the errors were reviewed, they were found to be oversights as the signs were definitely there. Some nontuberculous lesions, especially those at the base, were missed at first because too much concentration was given to the apical areas. Basal detail can

be obtained and interpreted when one has learned to distinguish between shadow differences in the miniature and in the regular films. The authors now apply the method to new patients coming to the tuberculosis clinic without taking a large film except when there is a questionable appearance in the small film. This has proved satisfactory in the two months during which 1,719 persons have been examined. The authors believe that the method can be carried out economically enough to make it practical in surveying large numbers without a preliminary tuberculin test, even in groups in which the reactor rate is low. There is need for only one visit by the patient. Only a few patients need to be reexamined, whereas with the preliminary tuberculin test at least two visits are required. There is always a loss growing out of the fact that many reactors fail to appear for x-ray examination. This amounted to 4,719 out of 31,803 reactors, or 14.8 per cent, in a recent study in Detroit. Most persons would rather have a roentgenogram taken than submit to a tuberculin test. There is also the possibility of detection of nontuberculous lesions of the heart and lungs. The cost of taking the 4 by 5 inch film is reasonable. These small films are easily handled, can be interpreted at the same speed as the large films, and require little space for storage. The method has definite advantages over full size celluloid films, sensitized paper films, full size films and 35 mm. films in accuracy, in cost or in both.

**Prognosis of Pulmonary Tuberculosis.**—Gershon-Cohen and Farrell investigated the prognostic possibilities of roentgenologic examination of tuberculous patients. They set up a standardization in diagnosis which included the extent and distribution of lesions, type of lesions and cavities. The changes on one side bear on those of the other side in a given relationship. The lesions were divided into four benign and four malignant groups. They have analyzed more than 600 cases and their preliminary estimate reveals that their prognoses were correct for approximately 80 per cent. In order to limit the analysis to the x-ray examination, the clinical picture and laboratory observations were excluded from all prognostic considerations. They believe that, when the same cases are reviewed to include these additional data, a better average of accuracy will be achieved. Their best prognoses were made in the more advanced benign and virulent groups. In the sanatoriums in which the analysis was made, most of the cases were benign or virulent to a moderate or advanced degree and the same held true in the dispensary practice. This would seem to reemphasize that, by the time the x-ray examination is asked for, pulmonary tuberculosis has passed beyond the early stages, in which event no one, the roentgenologist included, can foretell from a single examination the progress of the disease. Serial examinations can be resorted to and a fairly accurate prognosis arrived at in a few weeks.

## Surgery, St. Louis

**7:325-484 (March) 1940**

Histologic Study of Thyroid of Exophthalmic Goiter at Intervals During Administration of Iodine. W. D. Wilson, Marietta, Ga., and C. W. Mayo.—p. 325.
Progressive Postoperative Gangrene of Abdominal Wall: Case Report. H. J. Vier, White Plains, N. Y.—p. 334.
Keller Operation: Partial Phalangectomy in Hallux Valgus and Hallux Rigidus: Report of Fifty-Five Operations in Thirty-Two Cases. A. J. Schein, New York.—p. 342.
Principles Governing Treatment of Fractures and Bone Lengthening by Direct Skeletal Means and New Apparatus: Preliminary Report. E. J. Haboush, New York.—p. 356.
Artificial Skin-Lined Antethoracic Esophagus for Impermeable Stricture. A. H. Noehren, Buffalo.—p. 364.
Inquiry into Functional Capacity of Cecal Appendage in Representative Birds and Mammals. C. Dennis, R. E. Buirge and O. H. Wangensteen, Minneapolis.—p. 372.
Renal Venipuncture: Method of Explanation of Kidney for Venipuncture in Dogs. I. H. Page and A. C. Corcoran, Indianapolis.—p. 389.
Complete Recovery from Serious Vascular Impairment Following Removal of Cervical Rib. S. Silbert, New York.—p. 392.
Acute Free Perforation of Gallbladder Occurring Twice in Same Patient. E. I. Greene and G. C. Coe, Chicago.—p. 396.
Postoperative Simultaneous, Bilateral, Spontaneous Pneumothorax: Case Report. T. Golden, New York.—p. 401.
Recurrent Echinococcus Cyst of Thigh. J. B. Mason, Philadelphia.—p. 407.
Tidal Irrigator. E. P. Vary, Flint, Mich.—p. 410.
Localization of Occult Liver Abscess During Laparotomy Under Procaine Infiltration Anesthesia. E. S. Stafford, Baltimore.—p. 417.
Bilateral Extradural Hemorrhage: Case. P. A. Kunkel Jr., Harrisburg, Pa.—p. 420.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

## British Journal of Children's Diseases, London

**37:1-88 (Jan.-March) 1940**

*Nutritional Anemia: Further Survey of Debilitated Children in Manchester. Anne E. Somerford.—p. 1.
Diagnostic Errors. S. Wolff.—p. 16.
*Lederer's Anemia. F. R. B. Atkinson.—p. 35.

**Nutritional Anemia in Debilitated Children.**—Somerford reports on 201 children attending the outpatient department of the Royal Manchester Children's Hospital during 1938. The children were undernourished and appeared anemic but had no organic disease. Red cell counts of 4 million or less per cubic millimeter and 70 per cent or less of hemoglobin were considered as anemic. The ages of the children varied between 10 weeks and 13 years and 9 months. One hundred and seventeen, or 58.3 per cent, were found to be anemic with red cell counts between 3 and 4 million. Anemia was more prevalent in the male sex. About 45 per cent of the mothers were anemic. The red cells were chiefly normocytes with a mild degree of anisocytosis and poikilocytosis. Nucleated red cells were seen occasionally. The number of platelets was normal or increased. The leukocytes were within normal limits. Sixteen children and one mother had an anemia of the microcytic type such as may be associated with iron deficiency. The greater number of ill nourished children were among the wealthier families, but the proportion of anemic to nonanemic children was roughly the same in the three financial classes. Most of the children were breast fed. Exercise seemed to be fairly adequate in most cases, but it is doubtful whether hours of sleep were sufficient, particularly among the poorest. The size of the family had little effect on whether anemia was present or not. Vitamin C deficiency was found in twenty-one of sixty-three patients examined. Forty-one of the wealthier ones were deficient, twenty-two of the poorer class. Three factors appear to play a part in the production of malnutrition and nutritional anemia: 1. Poverty. 2. A slackening in home discipline, which permits the child to stay up late, and not to eat food he does not like; this factor accounts for the much larger percentage of vitamin-deficient children among the wealthier families. 3. Some psychologic influence; this is seen in anxious and hypersensitive children the offspring of nervous, highly strung mothers. The purely nutritional cases would be better off if dealt with away from the hospital atmosphere. After a preliminary examination to exclude the presence of disease, they should be returned to their welfare workers, women intimate with the home conditions and respected by the mothers.

**Lederer's Anemia.**—The literature on Lederer's anemia, according to Atkinson, comprises thirty cases in children and twenty-nine in adults. In most cases the disease begins acutely with exhaustion, profound asthenia, gastrointestinal symptoms, swelling of the abdomen, severe headache, pains in the limbs, tonsillitis and pharyngitis. An icteric tinge of the sclera and skin may be present. There is, as a rule, intermittent fever and chills. The urine is frequently yellowish from the presence of urobilin and may contain casts. Retinal hemorrhages with atrophy of the disks have been described. Hemic murmurs are often present. Hemoglobinuria was present in eleven of the thirty cases in children. The blood picture is characteristic. There is an acute hemolysis evidenced by hemoglobinuria, by hyperbilirubinemia, by increased excretion of urobilin in the urine and feces, by fragility of the erythrocytes and by the abnormally increased blood regeneration as revealed by the large numbers of reticulocytes and erythroblasts. The color index is often above 1. The hemoglobin is reduced in amount, the smallest recorded as low as 10 per cent. The red cell count is much below normal. Leukocytosis is nearly always present. The cause of hemolysis is a toxic factor the exact nature of which is unknown. Lederer's anemia is more frequent in the male, twenty-one and nine, respectively. The diagnosis is based on the acute onset, rapid anemia with no apparent cause, the evidence of hemolysis and the rapid cure resulting from transfusion. The outlook is grave if untreated but favorable if the proper treatment is instituted. Blood transfusion is the treatment of choice. Iron is of some value.

## British Medical Journal, London

1:471-516 (March 23) 1940

Chemotherapy of Clostridium Welchii Type A and Clostridium Septique Infections in Mice. Dora Stephenson and Helen E. Ross.—p. 471.
A Vascular Mechanism Related to the Great Vein of Galen. W. E. Le Gros Clark.—p. 476.
Mild Epidemic of Undulant Fever in a Boys' School Due to Drinking Raw Milk. G. W. Elkington, G. S. Wilson, Joan Taylor and F. Fulton.—p. 477.
*Subcutaneous Implantation of Female and Male Hormone in Tablet Form in Women. A. A. Loeser.—p. 479.
Sulfonamide Treatment of Bacterial and Trachomatous Conjunctivitis. A. F. MacCallan.—p. 482.
Epilepsy Treated with Epanutin. A. J. M. Butter.—p. 483.

**Subcutaneous Implantation of Hormone Tablets.**—Loeser implanted female hormone tablets in two women and male hormone tablets in ten. The two women in whom estradiol tablets were implanted had theretofore been sterile. Both had infantile uteri, desired children and had been treated unsuccessfully with female hormones and anterior pituitary lobe preparations. The result of the implantation was negative in the first patient, as the tablets were expelled ten days after their insertion, being implanted too near the skin. The large quantity of estradiol in the second patient depressed the function of the anterior lobe of the pituitary. As a result, maturation of the ovum and menstruation did not occur. Local action of estradiol on the uterine muscle and mucous membrane of the uterus became visible. The uterus grew and the mucous membrane became converted into cystically proliferated endometrium and was cast off gradually by hemorrhage. After the hormone tablets were removed the anterior lobe gradually recovered, the hibernating ovary was stimulated by fresh gonadotropic hormone produced in the anterior lobe, ripening of the ovum occurred again and hence there was normal menstruation. The muscular apparatus of the uterus had been substantially strengthened and was now able to draw up the semen, which it had previously been unable to do because of muscular deficiency. The patient became pregnant. Of the ten women given male hormone implants five had uterine fibroids, one functional bleeding, two chronically recurring mastitis and multiple nodules in the breast and two mammary cancer. The implantations controlled in some measure menorrhagia caused by fibroids in all the patients, and successfully in three. Male hormone did not influence existing recurrences of carcinoma of the breast following an operation or roentgen treatment. To what extent male hormone can have a prophylactic action against such recurrence is not yet determined. Improvement was obtained in the two women with chronic mastitis. All the patients acknowledged a feeling of well being, more balanced moods and clearer thinking, and some professed a greater determination.

## Indian Medical Gazette, Calcutta

75:65-128 (Feb.) 1940. Partial Index

Circulatory Failure in Typhoid Fever. G. Kelly.—p. 65.
Further Light on Mechanism of Sandfly Transmission of Kala-Azar. R. O. A. Smith, K. C. Halder and I. Ahmed.—p. 67.
Venom of Indian Cobra (Naja Naja) in Certain Painful Conditions. R. N. Chopra and J. S. Chowhan.—p. 69.
Observations on Pathology and Therapy of So-Called Frontier Sore (Second Communication). H. J. Hamburger.—p. 76.
Studies in Epidemiology of Plague in H. E. H. the Nizam's Dominions: Comparison of Certain Factors in Plague-Infected Place with That of Neighboring Plague-Free Area. S. Raghavender Rao.—p. 80.
Remarks on Etiology and Symptoms of Young-Dab-Hte (Neuralis): Report on Four Cases and Its Medicolegal Significance. R. M. L. Still.—p. 88.
Vitamin C and Ovulation. A. P. Pillay.—p. 91.
New Method of Treating Leukoderma. D. Panja and P. A. Maplestone.—p. 93.

## Journal of Hygiene, London

40:1-124 (Jan.) 1940

Notes on Preparation of Papers for Publication in the Journal of Hygiene and in Parasitology. G. H. F. Nuttall.—p. 1.
Scottish Cancer Mortality: Comparison of Urban and Rural Rates for Various Tumor Locations, 1931-1937, and a Survey of Recent Trends. R. S. Barclay and W. O. Kermack.—p. 63.
Poliomyelitis Epidemic of 1937 in Denmark: Epidemiology and Clinical Statistics. E. J. Henningsen and G. Rasch.—p. 84.
Serologic Investigation into Epidemiology of Influenza, with Particular Reference to Sporadic Cases. A. E. Martin.—p. 104.
Schick and Dick Reactions in Different Classes of Community. S. Thomson, A. J. Glazebrook and C. A. Green.—p. 115.
New Salmonella Type (Salmonella Rubislaw). J. Smith and F. Kauffmann.—p. 122.

## Lancet, London

1:533-582 (March 23) 1940

The Mystery of Alimentation. E. P. Catheart.—p. 533.
Transport of Wounded: Surgical Aspects. T. B. Layton.—p. 537.
Tumorigenic Powers of Stilbestrol and Follicular Hormones. A. Lipschütz and L. Vargas Jr.—p. 541.
Action of Veritol on Blood Pressure and Heart Under Various Anesthetics. G. Schoenewald, A. Schweitzer and G. C. Steel.—p. 544.
Spontaneous Hemothorax: Report of Case. M. Davidson and C. K. Simpson.—p. 547.
Further Case of Labyrinthectomy. M. Yearsley.—p. 548.

## Medical Journal of Australia, Sydney

1:325-360 (March 9) 1940

*Epidemiology of Poliomyelitis, with Special Reference to the Victorian Epidemic of 1937-1938. F. M. Burnet.—p. 325.
Some Problems of the First Year of Life and Their Management. F. N. LeMesurier.—p. 336.
The Sanatorium: Quo Vadis? A. H. Penington.—p. 341.

**Epidemiology of Poliomyelitis.**—Burnet reports the experimental work on the Victorian poliomyelitis epidemic of 1937-1938. The infection did not produce poliomyelitis antibody; certain children with initial antibody nevertheless suffered from paralytic infection. Cynomolgus monkeys could be infected with the local virus by ingestion or by pharyngeal swabbing. A study of the age incidence of poliomyelitis led to the conclusion that a change in the character of the disease has taken place in the last thirty or forty years. In the earlier period poliomyelitis was essentially an adult infection with incidental disorder of infants, while the present epidemic of poliomyelitis is a disease of childhood, spread by child contact. Poliomyelitis virus strains derive eventually from a virus which, prior to the end of the nineteenth century, was responsible for frequent infections of some part of the nasopharyngeal mucosa. Occasionally primary infection by the virus in unimmunized persons resulted in spread of the virus to the central nervous system and clinical paralysis. This happened only on first infections which, owing to the wide diffusion of the virus, could naturally occur only in very young children giving rise to the name "infantile paralysis." At this period the virus was capable, as influenza virus is today, of producing superficial infections in adults or older children with a basic immunity from former infection. This immunity was sufficient to prevent the spread of the virus to the central nervous system. With the advance of modern sanitation, opportunity for the free diffusion of the virus became more limited and a larger proportion of children passed through infancy without being infected. This provided a new means of spread for the virus by contact of susceptible children instead of transfer between partially immune adults. In this new biologic environment the virus gradually changed its character, becoming more infectious for children, less capable of infecting adults and more highly neurotropic. When the neurotropism is high, recent strains appear to be capable of overcoming an immunity which would have provided a solid protection against paralytic infection by strains of the earlier type. The present situation in a community such as Victoria is that there is probably still a good deal of the old type poliomyelitis virus infection, but that this is diminishing and is not often transferred to infants. The dominant strains are now spread like measles, essentially by child contact. A single infection does not provoke the appearance of antibody, and immunity to reinfection is probably only temporary. Previous infection with an antibody-producing strain does not insure immunity from paralysis by an epidemic strain. Infection occurs by inhalation or ingestion of contaminated saliva from an infected child. The primary focus is probably produced in the pharyngeal mucosa, and infection may reach the central nervous system by a variety of nerve paths. The olfactory route is probably an unusual one. Resistance to paralysis by epidemic strains develops with age, irrespective of specific immunologic factors. The Australian experience is that resistance to paralysis is greater in the warmer regions and that even a highly virulent strain may produce a small proportion of paralysis. For as yet unexplained reasons an epidemic may cease before all the susceptible population has been involved. On this basis the outlook for controlling the disease is not promising. Control by individual protection, vaccination, passive protection with human serum, chemical blocking of the olfactory area and protection by public health measures are all wanting. A close

investigation of the influence of climate and other environmental factors on the course of epidemics might suggest practical measures of individual protection. As epidemics nearly always terminate with the onset of cold weather, a "slowing down" of the epidemic by isolation and restriction of the aggregation of children may result in a large number of the susceptible being still untouched when climatic or other nonspecific factors terminate the epidemic. In six Melbourne districts during the 1937-1938 epidemic it was evident that every effort for the isolation of young children should be made to prevent infection.

## South African Medical Journal, Cape Town

14:65-84 (Feb. 24) 1940

Torula Meningitis, with Special Reference to Laboratory Findings: Two Cases. F. C. Gray.—p. 65.
Medical Establishments and Institutions at the Cape. P. W. Laidler.—p. 71.
William John Burchell: His Experiences as Consulting Physician While in Interior of Southern Africa, 1810-1815. Helen M. McKay.—p. 78.
Some Clinical Aspects of Tick Relapsing Fever in Natives in South Africa. D. Ordman and F. R. Jones.—p. 81.
Consideration of Life Cycle of Fasciola in South Africa. F. G. Cawston.—p. 84.

## Chinese Medical Journal, Peiping

57:1-100 (Jan.) 1940

Metastatic Tumors of Heart: Report of Two Cases Diagnosed Clinically. J. C. Hsiung, C. Szutu, C. K. Hsieh and V. T. Lieu.—p. 1.
*Medulloculture in Diagnosis of Typhoid and Paratyphoid Fevers: Analysis of Thirty-Eight Cases. C. C. Ling, S. S. Tsur, P. C. Hsueh and S. Y. Yang.—p. 11.
Positive Medulloculture in Staphylococcic Septicemia: Report of Case. C. C. Ling, P. C. Hsueh, S. S. Tsur and S. Y. Yang.—p. 27.
Transmission of Malaria Among Drug Addicts in Peiping: Demonstration of Malarial Parasites in Syringes Used for Intravenous Injections of Heroin. H. L. Chung, W. T. Liu, C. W. Wang and I. Chu.—p. 32.
Nonmetric Morphologic Characters of the Western Chinese Skulls. C. S. Lu.—p. 39.
Culture of Richettsiae of Chinese Typhus in Yolk Sac of Developing Chick Embryo. J. Tchang and G. B. Mathews.—p. 47.
Use of Purified Protein Derivative in Tuberculin Patch Test. G. Ouyang.—p. 51.
Malaria in Western Yunnan, with Reference to the China-Burma Highway. R. C. Robertson.—p. 57.
Some Experiments on Resistance of Larvae of Latrine Fly, Chrysomyia Megacephala, Against Chemicals. H. M. Jettmar.—p. 74.

**Medulloculture in Diagnosis of Typhoid and Paratyphoid.**—Ling and his colleagues made a detailed study of medulloculture in thirty-eight patients suffering from typhoid and paratyphoid. Of 110 medulloculutres and an equal number of hemocultures performed on the thirty-eight patients, both showed positive growth in thirty-one instances and negative in thirty-three. Medulloculture yielded a positive growth in forty-four instances in which a hemoculture was negative. Only two medulloculutres failed to demonstrate the organism in which hemoculture was positive. The average time required for growth in medulloculutres was shorter than for blood cultures, indicating heavier infection with more organisms in the bone marrow than in the blood. Medulloculture makes earlier bacteriologic confirmation of the clinical diagnosis possible. In typhoid the main agent of defense is the reticulo-endothelial cell. Since the bulk of reticulo-endothelial tissue is situated in the bone marrow, spleen and liver, not only are the characteristic pathologic changes to be found there but the invading organisms as well. Most of the positive growths from the sternal marrow and blood occur during the febrile period. With medulloculture the organisms may still be isolated when the temperature has been normal for two weeks. This persistence of the bacillus in the bone marrow may explain the relapses of typhoid and paratyphoid. The bone marrow serves as a depot of Bacillus typhosus and Bacillus paratyphosus to the circulating blood. The presence of bacilli in the bone marrow is not responsible for the clinical symptoms although it undoubtedly signifies active infection. But when the bacilli are liberated into the blood stream and endotoxins are set free, the foreign proteins in the blood give rise to fever and other symptoms and signs of toxemia. Medulloculture has thus possibly opened a new field in clinical investigation of typhoid by enabling one to determine the possibility of relapse. An etiologic diagnosis may still be established in patients seen for the first time as late as two weeks after the acute stage is over.

## Gynécologie, Paris

38:517-564 (Sept.-Oct.) 1939

*Diethylstilbestrol, Synthetic Estrogenic Substance. J.-A. Huet, R.-J. Comte and A.-D. Herscberg.—p. 517.
Grave Familial Icterus of the Newborn: Case. H. Vertruyen, F. Lévy and L. Vandiest.—p. 553.

**Diethylstilbestrol, Synthetic Estrogenic Substance.**—Huet and his associates employed diethylstilbestrol in forty-six cases of gynecologic disorder. The substance was found to be effective in genital infantilism, in certain forms of oligomenorrhea and dysmenorrhea, in functional disorders of the menopause and in a number of hypophysio-ovarian disturbances. The treatment was successful in 77 per cent of the cases of menstrual dysfunction and in 82 per cent of menopausal disturbances. In the latter it counteracted the hot flushes, the profuse sweats and the vasomotor symptoms. The untoward secondary effects of this treatment were few. In 10 per cent of the cases the complications were benign. They consisted of attacks of weakness and nausea, which disappeared in the course of treatment. These complications were observed especially in women of the premenopausal and menopausal age. In about 3 per cent of the cases total gastric intolerance existed but its symptoms ceased when the medication was discontinued. The therapy with the synthetic estrogenic substance has advantages over that with the natural estrogens. Diethylstilbestrol is highly effective when administered by mouth, is easily handled and is relatively inexpensive. The fact that it is a powerful therapeutic agent necessitates an exact etiologic diagnosis and close clinical supervision in order to avoid disappointments. The authors recommend a dosage of 2 mg. of diethylstilbestrol daily given in two doses (morning and evening), far from meals, from the eighth to the eighteenth day, counting from the first day of the menstrual period. If an immediate menstrual flow is the object, the substance can be given for three days before the presumed onset of menstruation in a dose of 5 mg. daily. In the presence of hypophysio-ovarian disturbance 3 mg. daily for three days is recommended, beginning with the second day of menstruation. In cases of dysmenorrhea caused by uterine hypoplasia, 5 mg. is given on the day before the onset of the menstrual flow. In certain oligomenorrheas the dose is reduced to 1 mg. daily for ten days, in order to avoid too abundant hemorrhages.

## Gynécologie et Obstétrique, Paris

40:283-394 (No. 4) 1940. Partial Index

"True Prolonged Pregnancies" and Their Significance. A. Fruhinsholz and J. Richon.—p. 283.
Parturition in Sportswomen. J.-L. Audebert.—p. 294.
Endometriosis and Pregnancy. L. Portes and J. Varangot.—p. 298.
Anatomoclinical Classification of Cervicitides. P. Durel, V. Ratner and A. Derois.—p. 305.

**Prolonged Pregnancy.**—Fruhinsholz and Richon discuss the etiology of prolonged pregnancies, with special reference to familial and individual involvements, on the basis of 128 (0.65 per cent) cases in 19,893 deliveries, thirteen (1 per cent) of the cases terminating fatally. Only those pregnancies were considered as prolonged that extended beyond the 300th day after the last verified menstruation, with a maximal terminal range of 351 days. Ninety-two deliveries (about 72 per cent) occurred between the 301st and 314th day, one on the 351st day. The authors regard prolonged pregnancies not merely as accidental variations of normal pregnancies but as possessing distinct pathologic implications, discoverable in the family and personal history of the patient. Among the pathologic factors observed in eighty-one (63 per cent) of the cases were found premature deaths and insanity (fourteen cases), multiple infant mortality (27.7 per cent) and coexisting physical abnormalities such as obesity, strabismus, exophthalmic goiter and epilepsy in sixteen cases. The body weight of the children at birth exceeded normal standards (in seventy cases it was between 3,000 and 6,000 Gm.) but no correlation was noted between greater body weight and deaths (the child weighing 6,000 Gm. died in utero). Placental weight likewise showed a higher curve. In fifty-five cases it was between 600 and 1,000 Gm. Infant mortality (10 per cent) in overdue pregnancies also surpassed the normal death rate, was equally divided between male and female infants but stood in no relation to the number of days of the child's intra-uterine existence. No deaths were due to obstetric interventions of a

mechanical nature. The personal history of the patients disclosed delayed initial menstruation (in thirty-nine cases between the fifteenth and twenty second year) and delayed conception (in twenty-three of thirty-four primiparas from six months to five years after marriage, once after thirteen years). These retardations are attributed by the authors to an endocrine insufficiency of a hypophysial character. The average duration of labor was also higher, from eighteen to twenty-one hours in primiparas, ten and one half hours in multiparas. Only six of the 128 patients reacted positively to the Wassermann test. Yet syphilis, though inconspicuous in the clinical picture, is believed by the authors to be ultimately and hereditarily chargeable with the various familial and individual pathologic conditions noted in these cases. Fetal malformations were relatively frequent. Tuberculosis and alcoholism were infrequently observed. Primiparity and multiparity were found etiologically to be of no significance. Intervention was resorted to only in exceptional cases and was limited to endocrine medication.

## Presse Médicale, Paris

**48:233-248 (Feb. 28-March 2) 1940**

Reflections Preparatory to Experimental Research on Rôle of Sympathetic in Articular Pathology. S. de Sèze, G. Guiot and J. Serane. —p. 233.

*Oral Treatment of Trachoma with P-Aminophenylsulfamide. F. Jasseron and G. Morard.—p. 234.

*Sulfanilamide Derivatives in Treatment of Trachoma. L. Poleff.—p. 235.

*Improved Process of Method of Armand-Delille to Determine Presence of Koch Bacilli in Gastric Contents. L. Koganas and D. Nakanas. —p. 236.

**Oral Treatment of Trachoma with P-Aminophenylsulfamide.**—Jasseron and Morard call attention to oral treatment of trachoma with p-aminophenylsulfamide and point out that in their experience this substance showed the best results in the chemotherapeutic treatment of trachoma. The authors treated nearly 200 patients. Subjective symptoms, such as pain, photophobia and lacrimation, disappeared in forty-eight hours; pannus and infiltration of the cornea were resorbed in eight days; corneal ulcers acquired epithelium in thirty-six hours; cicatrization was accelerated and clinical recovery took place in three weeks in 75 per cent of the cases. Secondary infections with Weeks's bacillus, diplobacilli of Morax, pneumococci and gonococci were sterilized in four days. The authors recommend for adults ingestion of 20 Gm. in thirteen days, for children aged from 8 to 12 years 12 Gm. in twelve days, and for children aged from 4 to 8 years 7 Gm. in twelve days in decreasing dosage. Limited local treatment is advised.

**Sulfanilamide Derivatives in Treatment of Trachoma.**—According to Poleff, instillation of sulfanilamide derivatives into the eye caused conjunctival hyperemia with dilatation of the vessels, while subconjunctival injections were followed by intense hemorrhage at the place of injection. Repeated instillations and subconjunctival injections in five cases were not followed by sterilization of the bacterial flora of the conjunctival sac, while silver nitrate and ethoxydiamino-acridine lactate produced rapid diminution of the bacteria and general improvement. Intramuscular injections alternated with oral administration of sulfanilamide derivatives were followed by notable decrease of bacteria in the conjunctival sac; however, the final results were not satisfactory. Oral and intramuscular administration of sulfanilamide derivatives together with the usual treatment of trachoma produced very satisfactory results in fifteen malignant cases. Pallor and rapid loss of weight in the course of sulfanilamide therapy are symptoms of intolerance to the drug.

**Improved Method of Determining Tubercle Bacilli in Gastric Contents.**—Koganas and Nakanas point out that tuberculous patients do not always expectorate but may swallow their sputum or else scanty pulmonary secretion may get into the stomach without provoking a cough. A considerable number of patients have Koch bacilli in the stomach. Examination of the gastric contents by the improved Armand-Delille method renders quick diagnosis possible. The method consists of examining the stained centrifuged residue of the gastric contents. In the absence of typical bacilli the residue is thoroughly mixed with equal parts of 4 per cent sodium hydroxide and after centrifugation the residue is neutralized with hydrochloric acid. Part of this is dried and is examined for Koch bacilli while the rest is cultured or injected into guinea pigs. The authors examined 115 tuberculous patients with this method and found Koch bacilli in the stomach of most patients who did not expectorate. In only 26 per cent of the examined cases were the authors obliged to culture and inoculate guinea pigs. The authors regard this method superior to laryngeal smear or stool examination.

## Monatschrift für Psychiatrie und Neurologie, Basel

**102:65-128 (No. 2) 1940**

*Contributions to Vaccine Therapy of Radicular Symptoms in Tabes. L. von Angyal and K. Gyárfás.—p. 65.

Psychopathology of Simple Schizophrenias. J. Wyrsch.—p. 75.

Aspects of Extrapyramidal Motor System. E. Grünthal and K. Hartmann.—p. 107.

**Vaccine Therapy of Radicular Symptoms in Tabes.**—Von Angyal and Gyárfás used Hitgermann's spirochetal vaccine in nineteen cases of locomotor ataxia. The vaccine was injected subcutaneously into the anterior part of the thigh at intervals of two weeks. The initial dose was from 0.5 to 1 cc. When the reaction was too severe, the dose was reduced to 0.1 or 0.2 cc. The total number of injections varied between one and twelve. Reflex disturbances such as hypotonia and dysuria did not respond to the treatment. Complaints ascribed to radicular irritation reacted well. Shooting pains, present in fifteen cases, ceased altogether in five and were improved in nine. Gastric crises (eleven cases) responded nearly as well; they stopped altogether in two cases and there was an improvement in seven. Vesical and intestinal crises (one case each) were controlled for the time being. The impression was gained that intense local or focal reaction constitutes a favorable sign.

## Policlinico, Rome

**47:389-432 (March 11) 1940. Practical Section**

*Treatment of Suppurative Mastitis and Acute Abscesses Without Incision. E. Pagliai.—p. 389.

Septicemia from Streptococcus Viridans of Dental Origin Without Endocarditis: Recovery of Patient. A. Fabris.—p. 403.

**Treatment of Suppurative Mastitis Without Incision.**—The treatment advised by Pagliai consists of repeated puncture of a breast abscess, aspiration of pus and injection into the cavity of an ointment made up of equal parts of pure cod liver oil and white petrolatum. He has obtained satisfactory results from this treatment in more than 100 cases. The first puncture is made with the aid of a 1 per cent procaine hydrochloride anesthesia of the superficial and deep tissues about the abscess. The following punctures are made through the route followed by the needle in the first puncture. The treatment is repeated every other day. It is discontinued altogether as soon as secretions assume a sanguineous appearance. Lactation is temporarily discontinued but is preserved. The breast is emptied every three hours with a breast pump and is dressed with warm wet compresses. If the nipple is fissured it is gently washed with boiled water after each withdrawal of milk and is dressed with cod liver oil ointment. As a rule, acute suppurative mastitis is controlled by this treatment in from one to two weeks, after which lactation is recommenced. Repeated puncture of the abscess, aspiration and injection of cod liver oil ointment gave prompt satisfactory results in acute abscesses and acute suppurative lymphadenitis.

## Arch. f. Ohren-, Nasen- u. Kehlkopfh., Berlin

**147:1-68 (Jan. 9) 1940**

Antagonisms of Reflexes of Neck and of Semicircular Canals in Movements of Human Eyes. A. Güttich.—p. 1.

Clinical Aspects of Tumors of Fourth Ventricle, Determination of Direction of Bound in Case of Intact Cochlear and Missing Vestibular Nerve. A. Güttich.—p. 5.

Diagnostic Value of Oto-Audion in Hardness of Hearing with Normal Tympanic Membrane. W. Herrmann.—p. 8.

*Combination of Pigment Degeneration of Retina with Deaf-Mutism. H. Weber.—p. 38.

Pulsating Mucocele. H. Richter.—p. 61.

Orbital Emphysema Caused by Fracture of Ethmoid Bone After Head Hit Surface of Water During Diving. A. Meyer zum Gottesberge. —p. 66.

**Pigment Degeneration of Retina with Deaf-Mutism.**—Weber discusses the question of the combined appearance of degeneration of the pigment of the retina with deaf-mutism being due to an internal causal connection or to hereditary anomalies

existing side by side. A family in which pigment degeneration and deaf-mutism concurred was studied. The genealogic tree of the family failed to furnish an answer to the question of how the combined two disorders were to be explained. It is noteworthy that the siblings who are affected suffer from the two disorders simultaneously. This combined appearance creates an impression that the two defects belong together, the more so since in the three cases in which the defects occurred the vestibular nerve did not respond to stimulation. However, the assumption of the common origin of the two hereditary disorders is contradicted by the fact that the pigment degeneration of the retina has been known to concur not only with the recessive deaf-mutism but also with the dominant hardness of hearing of the inner ear. The combination of deaf-mutism with pigment degeneration has raised the question of whether it is due to a hereditary combination elicited by a common gene. The opinions on this subject are contradictory. The author reviews the factors cited in favor of a unitaristic origin as well as those favoring a separate and independent hereditary transmission. Indicative of an independent hereditary transmission are the essential difference of deaf-mutism and pigment degeneration, the fact that in most instances the two disorders appear separately and that the combination is the exception, the promotion of the combination by blood relationship of the parents, the concurrence of feeblemindedness with one or the other or with both of the defects and the occurrence of other combinations. Nevertheless the author feels that the acceptance of an independent and separate hereditary transmission must be made with reservations, because the examined material is insufficient to permit a complete survey of the problem. The final answer will probably be similar to that given by Siemens, namely that the apparent correlation of recessive hereditary defects in the children of parents related by blood is due to identical descent, because, since all recessive defects are more frequent with inbreeding, it is self evident that they frequently concur among siblings or even in the same person.

## Zeitschrift für Immunitätsforschung, Jena

**97:273-364 (Jan. 7) 1940. Partial Index**

Experimental Investigations on Serologic Characteristics of Fraenkel's Gas Bacillus (B. perfringens). F. Nagler.—p. 273.
Role of Antigen Vi in Variation of Typhoid Strains. K. Rauss.—p. 281.
Investigations on Passive Active Immunization Against Diphtheria. I. Fjord-Nielsen.—p. 306.
Comparative Investigations on Toxic and Antigenic Characteristics of Soluble Bacterial Constituents Obtained at Low Temperatures from Typhoid, Paratyphoid, Enteritis and Dysentery Group. R. Hass.—p. 317.
Heuristic Theory of Manifestations of Immunization and Anaphylaxis. P. Jordan.—p. 330.
*Experiences and Results with Chemotherapeutic Modification of Venereal Lymphogranuloma and Other Virus Diseases. F. Bär.—p. 344.

**Chemotherapy of Venereal Lymphogranuloma and Other Virus Diseases.**—Bär resorted to intracerebral inoculation of mice with emulsions of the brain substance of mice that had a severe form of venereal lymphogranuloma. The comparative study of various derivatives of the sulfanilamide group was done by repeated subcutaneous injections of the preparation to be tested. The first dose was usually administered one hour after the infection with the virus of venereal lymphogranuloma. The results of the investigations are recorded in graphs, which reveal that a number of sulfanilamide preparations exert a chemotherapeutic influence on experimental venereal lymphogranuloma. Among the large number of preparations tested, the most effective were dimethyldisulfanilamide, monomethyldisulfanilamide, and disulfanilamide, azosulfamide, a soluble form of the latter, benzylsulfanilamide, sulfapyridine, the azo body 33 of Girard and others. The repeated administration of these compounds either prolonged the life of the animals or produced complete survival, in contradistinction to the untreated animals, which generally died. After pointing out that the sulfanilamide preparations have been found effective also in human infections with venereal lymphogranuloma, the author suggests that the therapeutic action is probably due to the fact that the injected preparation inhibits the development of the virus and that after this impairment the defensive powers of the organism complete the destruction. The author was able to corroborate the observation that in some of the animals the virus remains viable for a time after the administration of the preparation and that some of the animals which were cured developed an active immunity against a renewed inoculation with the virus of venereal lymphogranuloma. The critical evaluation of results obtained thus far by various investigators in the chemotherapy of virus diseases show that only in venereal lymphogranuloma, in trachoma and in certain symptoms produced by the Rickettsia group of organisms can a noticeable therapeutic effect be observed; all other experimental results still lack verification.

## Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

**84:905-1012 (March 9) 1940. Partial Index**

Task of Internist in Treatment of War Injuries. J. G. G. Borst and H. P. Veeming.—p. 914.
*Development of Resistance to Sulfapyridine in Strains of Pneumococci in Vivo. J. Mulder, R. van den Berg and G. Eimers.—p. 923.
*Saline Enema in Postoperative Intestinal Paralysis. J. J. Suren.—p. 928.
Endophlebitis Hepatica Obliterans. P. Formijne.—p. 932.
Synthetic Estrogenic Substances in Gynecology. W. M. J. Schellekens.—p. 940.

**Resistance to Sulfapyridine in Pneumococci.**—Mulder and his associates demonstrated in experiments on mice that a strain of pneumococci (type I in America) which is highly sensitive to sulfapyridine may rapidly develop a resistance against that substance. At first the resistant strain is less virulent than the sensitive strain, but after a few mouse passages it regains its maximal virulence. Resistance may be complete in the presence of full virulence. In the early stages of resistance the strain may cause a prolonged bacteremia in spite of treatment with sulfapyridine; later this phenomenon disappears. The possibility of the development of a resistance to chemotherapy must be considered in the clinic. Severe pneumococcic infections should be treated from the onset with large doses of sulfapyridine, and type specific antiserum could perhaps be combined with it.

**Saline Enema in Postoperative Intestinal Paralysis.**—The large number of remedies recommended to stimulate peristalsis in postoperative ileus indicates, according to Suren, the inadequacy of these measures. A comparatively simple and yet highly effective procedure employed by Stahnke in Ludwigshafen, also described by Genkin and Miljawskaja (*Arch. f. klin. Chir.* **176**:156 [Aug. 24] 1933; abstr. THE JOURNAL, Nov. 4, 1933, p. 1521) was employed by the author in several hundred cases. Two tablespoons of sodium chloride is dissolved in 150 cc. of lukewarm water and introduced as a drop enema high into the rectum. The enema may be effective before it has been completed, frequently after five minutes and always within fifteen minutes. However, the sodium chloride enema remains ineffective when a mechanical obstruction exists. In such cases the enema is repeated after an hour and, if ineffective, surgical treatment is decided on. Thus the sodium chloride enema is also of value in the differential diagnosis. The method had not received the attention it deserves.

## Nordisk Medicin, Gothenburg

**8:117-164 (Jan. 27) 1940. Partial Index**

### Hospitalstidende

Hernias of Omental Bursae (Together with Report of Case of Transmesocolic Hernia of Omental Bursa). J. C. Christoffersen.—p. 117.
Duodenojejunal Hernias (Together with Report of Case of Treitz's Hernia). O. Povlsen.—p. 122.
Determination of Serum Phosphatase and Serum Citric Acid in Disorders of Liver and Biliary Tract. (Preliminary Report.) H. Buch.—p. 125.
*Value of Takata Reaction in Hepatic Disorders. E. Godtfredsen.—p. 131.

**Takata Reaction in Hepatic Disorders.**—Godtfredsen finds that a positive Takata reaction, when disorders with hyperglobulinemia, which are relatively rare, can be excluded, points to parenchymatous injury of the liver. The reaction is negative in even long-continued obstructive jaundice. In cirrhosis the reaction is positive in between 90 and 95 per cent of the cases, often in marked degree. In acute hepatitis the test is useful in prognosis, a continued negative result during the first ten days after appearance of the jaundice indicating a favorable course; conversely, a positive reaction is most often seen in cases in which the possibility of transition into chronic hepatitis (cirrhosis) is likely.

# THE STUDENT SECTION

of the

## Journal of the American Medical Association

*Devoted to the Educational Interests and Welfare of Medical Students, Interns and Residents in Hospitals*

SATURDAY, MAY 25, 1940


## An Organized Educational Service for Interns


ARTHUR H. WELLS, M.D.

From the Department of Pathology, St. Luke's Hospital.

DULUTH, MINN.


One of the important trends in medical education today is forecast by an unusual interest and activity of medical organizations in the improvement of postgraduate training and especially of internship training. The ever increasing pressure of the American Medical Association combined with a rapidly growing interest of medical school authorities in behalf of their graduates will undoubtedly bring about widespread changes in this field of education. The growing disparity between the number of internships and the available interns for these positions is being used as an effective lever for bringing about the realization of a more extensive teaching responsibility on the part of hospital authorities.

Even as a medical school predetermines the nature of its graduates, so a hospital must plan its educational program knowing the purpose of its efforts. Internships of the general rotating type must of necessity be designed to train men for the general practice of medicine. To this end, emphasis must be placed in the fields of internal medicine, surgery, obstetrics, pediatrics and clinical pathology. To best motivate such a program, an inspiring teacher in each of these branches of medicine should be in a controlling position and assume much of the responsibility of providing a minimum of instruction in a given specialty and at the same time collaborating with the other four teaching supervisors.

It must be assumed that the intern has covered the field of didactic medicine and that he is now ready to learn how to apply himself. There is no question that this is best accomplished by his own efforts in attacking one diagnostic and therapeutic problem after another guided by the constant criticism of attending physicians. To facilitate this better in our private hospital, where it is impossible for the intern to make rounds with more than a few of the 125 staff physicians, a special "Interns' Educational Sheet" is inserted in each chart. Questions, comments and personal notations are put on this sheet including the interns' suggested diagnostic procedures and therapy. The sheet is later removed from the chart and given to the intern. The interns are required to make routine progress notes on all patients. Furthermore, meetings are scheduled during the year at which the individual supervisors of intern instruction review many selected charts of discharged patients, criticizing the interns' notes with a free hand and at the same time making important practical observations.

### A SCHEDULE OF CONFERENCES

In the majority of private hospitals and even in many teaching institutions, too much is being left to chance and the initiative of the intern. A schedule of a minimum number of talks or conferences covering applied medicine for the general practitioner should be drawn up by the supervising committee (a sample schedule is shown at the end of the article). This will not interfere in the slightest with the additional self-educational efforts of those interns endowed with sufficient interest, initiative and energy. In fact, it will stimulate the less inclined to a greater activity in the art of medicine. By concentrating pertinent subjects in the first few weeks of the internship, we hope to train good interns. After that the talks are scheduled every Monday and Tuesday at 5 p. m. Subjects directly related to his imminent entrance into general practice are concentrated mainly during the last two months. Every effort is made to avoid formal lectures. The subjects of different specialties are intermixed with the hope of teaching the student how to study diseases in the disorderly manner in which they will be presenting themselves in general practice. In a private hospital the responsibility for these many conferences is best spread widely among those members of the medical staff who are most suited for the subjects, rather than putting too great a burden on a small group. We have distributed the number of subjects in the various specialties as follows: medicine twenty-five, surgery twenty, obstetrics eleven, pediatrics six,

roentgenology ten, other specialties fifteen and miscellaneous fifteen.

Thursday evenings, throughout most of the year, are devoted to interns' clinical-pathologic conferences at which the interns rotate in presenting the more difficult diagnostic cases which they have helped study. Each case is discussed in great detail. About fifteen minutes is devoted to projecting the more important tissue sections from autopsy and surgical specimens of the preceding week on a screen with a brief comment on clinical and pathologic manifestations. Staff physicians attend these informal meetings and join in the discussions.

Each intern is scheduled to review the hospital's medical periodicals during an assigned month. Lively and stimulating comments will frequently develop between interns and staff physicians at these seminars.

The interns give case presentations at our monthly clinical-pathologic conferences before a large group of physicians. The training is valuable and even with this limited experience there is a decided improvement in the intern's ability to prepare for and speak before a formal gathering. His required attendance at monthly staff meetings not only has its scientific values but also gives him an immediate understanding of the importance of organization and cooperation with his fellow practitioners.

### RATIO OF INTERNS TO ADMISSIONS

The most serious error a hospital can make is to have too few interns for the volume of work expected of them. This type of exploitation makes acceptable work impossible and stifles individual initiative. We feel that nine interns is a minimum number for our close to 7,000 hospital admissions. The Council on Medical Education and Hospitals advises one intern for every 500 admissions. On the other hand, there may be such a thing as having too many interns.

A word should be said on the importance of two features of the hospital's laboratory service in relation to intern training, a field sometimes sadly neglected. Our interns obtained permissions for necropsies on 75 per cent of the hospital deaths last year principally because of what they learned from the discussions on both clinical and pathologic aspects of each case at the autopsy table. Frequent demonstrations of practical anatomy add to the intern's dividends. Special sessions are scheduled each year for surgical technic on cadaver material demonstrated by a surgeon. The intern in the laboratory service is encouraged to replace the diener and sew up the necropsy incisions using surgical technic and materials. These practices are not intended to make surgeons out of our house officers; in fact, it is very likely that they will not be permitted to perform a single major operation during their internship.

It is fundamental to the type of medicine practiced in a hospital and therefore to the teaching of interns to remove the financial barrier of laboratory costs. A flat rate fee of from $3 to $5 in a hospital admitting 3,000 or more patients a year will cover all laboratory tests and will provide a service equal to that of larger medical centers for physicians, their poorest patients, and interns.

### SUMMARY

Hospitals accepting the responsibility of intern training should be considered extensions of medical schools and should adapt many of their methods of teaching. Where an internship is of the general rotating type, a controlling group of teachers in the fundamental subjects of medicine, surgery, obstetrics, pediatrics and clinical pathology should arrange a schedule of conferences, seminars and medical meetings as much as a year in advance. The curriculum should stress only those subjects which will be of practical value to a general practitioner of medicine. To become a specialist in any field, three or more years of additional training is necessary. As to the numerous details of arranging a comprehensive program of this nature, there should be considerable leeway to allow for local peculiarities. However, lax methods, leaving too much to chance and the initiative of the intern, must give way to orderly, planned teaching methods, and the common practice of exploitation of interns must cease.

### SCHEDULE OF REQUIRED CONFERENCES, SEMINARS AND MEDICAL MEETINGS FOR INTERNS

(Time 5 to 6 p. m. unless scheduled otherwise)

July 1. Superintendent's introduction. Mr. James McNee

2. Introduction to surgical department; gastric decompression, hypodermoclysis, intravenous therapy, rectal tube, Miller-Abbott tube, proctoclysis, surgical dressings. Dr. K. E. Johnson

3. Surgical technic and surgical intern; conduct of operating assistants. Dr. T. L. Chapman

5. Miscellaneous technic: circumcisions, transfusion, spinal puncture, oxygen therapy. Dr. Stewart Clapp

8. Introduction to obstetric department; delivery room technic. Dr. R. J. Moe

9. Introduction to laboratory department; functions of the laboratory intern, mimeographed directions for common tests, location of apparatus and reagents. Dr. A. H. Wells

10. Introduction to pediatric department; pediatric history, physical examination. Dr. E. E. Barrett

11. Orthopedic apparatus and its application (demonstration). Dr. M. H. Tibbetts

12. Neurologic and psychiatric examination and history. Dr. L. R. Gowan

15. Malpractice suits. Mr. John J. Fee

16. Recognition and treatment of shock. Dr. P. S. Rudie

17. Postoperative treatment in abdominal surgery. Dr. C. H. Mead
18. Diabetic emergencies. Dr. D. W. Wheeler
19. Caldwell and Molloy pelvimetry. Dr. K. E. Johnson
22. Organic and postpartum uterine bleeding. Dr. W. A. Coventry
23. Treatment of burns and skin grafting. Dr. F. J. Elias
29. Significance of hematologic tests. Dr. A. H. Wells
30. Care of the premature. Dr. W. C. Martin

Aug. 5. X-ray demonstrations of diseases of skull, mastoids and sinuses. Dr. Gage Clement
6. Anesthetics and analgesics during labor. Dr. P. N. Bray
12. X-ray demonstration of bone fractures. Dr. Gage Clement
13. Hospital medical literature review for July. J. J. Halbert
19. X-ray demonstration of bone tumors. Dr. Gage Clement
20. Stricture of esophagus and alkaline management of peptic ulcers. Dr. L. L. Merriman
26. X-ray demonstration of diseases of stomach and esophagus. Dr. Gage Clement
27. The hemorrhagic diseases. Dr. W. D. Coventry

Sept. 2. X-ray demonstration of diseases of intestinal tract and gallbladder. Dr. Gage Clement
3. The acute surgical conditions of the abdomen. Dr. L. A. Barney
5. Interns' clinical-pathologic conference; case presentation. W. F. Vaudreuil
9. X-ray demonstration of diseases of genito-urinary tract. Dr. Gage Clement
10. Review of medical charts to date. Dr. S. H. Boyer Jr.
12. Interns' clinical-pathologic conference; case presentation. E. C. Strauss
16. X-ray demonstration of pulmonary tuberculosis. Dr. Gage Clement
17. Care of the feet. Dr. R. T. Seashore
19. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
23. X-ray demonstration of other lung diseases. Dr. Gage Clement
24. Review of surgical charts to date. Dr. K. E. Johnson
26. Hospital medical literature review for August. E. Emerson
30. X-ray demonstration of diseases of the heart and mediastinum. Dr. Gage Clement

Oct. 1. Surgical treatment of pulmonary tuberculosis. Dr. A. Hedberg
2. Monthly pediatric-pathologic conference, 5:15.
3. Interns' clinical-pathologic conference; case presentation. E. Steiger
7. X-ray demonstration of miscellaneous diseases. Dr. Gage Clement
8. Infant feeding. Dr. O. W. Rowe
10. Interns' clinical-pathologic conference; case presentation. D. R. Lannin
14. Surgical anesthesia. Dr. W. A. Swedberg
17. Monthly clinical-pathologic meeting, 7:20. Monthly hospital medical staff meeting, 8:20.
21. Review of pediatric charts to date. Dr. E. E. Barrett
22. Practical suggestions on syphilis. Dr. W. E. Hatch
24. Interns' clinical-pathologic conference; case presentation. W. K. Hartford
28. Dermatologic problems for general practitioners. Dr. F. T. Becker
29. Hypertension. Dr. S. G. Sax
31. Hospital medical literature review for October. William D. Cleaves

Nov. 4. Practical suggestions on diagnosis and medical treatment of pulmonary tuberculosis. Dr. A. T. Laird
5. Review of obstetric charts to date. Dr. R. J. Moe
6. Monthly pediatric-pathologic conference.
7. Interns' clinical-pathologic conference; case presentation. J. J. Halbert
11. Anemias. Dr. S. H. Boyer Jr.
12. Bright's disease in practice. Dr. Stewart Clapp
14. Interns' clinical-pathologic conference; case presentation. E. Emerson
18. Minor surgery. Dr. G. C. MacRae
19. Medical ethics, also the Harrison Act. Dr. F. H. Magney
21. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
25. Traumatic and common eye diseases (demonstration). Dr. M. F. Fellows
26. Actual preparation of diabetic diet (demonstration). Miss L. Almstrom
28. Interns' clinical-pathologic conference; case presentation. William T. Cleaves

Dec. 2. Actual preparation of other diets (demonstration). Miss L. Almstrom
4. Monthly pediatric-pathologic conference.
5. Hospital medical literature review for November. C. Christensen
9. Illustrated dermatologic diseases. Dr. E. Z. Shapiro
10. Diabetes mellitus. Dr. Richard Bardon
12. Interns' clinical-pathologic conference; case presentation. C. Christensen
16. Treatment of common cold and grip. Dr. S. H. Boyer Jr.
17. The prostatic patient. Dr. A. N. Collins
19. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.

Jan. 6. Toxemias of pregnancy. Dr. A. O. Swenson
7. Review of medical charts to date. Dr. S. H. Boyer Jr.
8. Pediatric-pathologic conference, 5:15.
9. Interns' clinical-pathologic conference; case presentation. W. F. Vaudreuil
13. Clinical electrocardiography. Dr. R. L. Nelson
14. Autonomic aspects of vascular balance. Dr. R. L. Nelson
16. Annual medical staff meeting, 7:30.
20. Spinal fluid examination; interpretation. Dr. A. H. Wells
21. Blood protein deficiency. Dr. S. H. Boyer Jr.
23. Hospital medical literature review for December. W. F. Vaudreuil

27. Gallbladder diseases. Dr. P. S. Rudie
28. Anal and rectal diseases. Dr. W. G. Strobel
30. Interns' clinical-pathologic conference; case presentation. E. C. Strauss

Feb. 3. Carcinoma of colon. Dr. L. A. Barney
4. Practical observations on head injuries. Dr. L. R. Gowan
5. Pediatric-pathologic conference, 5:15.
6. Interns' clinical-pathologic conference. E. Steiger
10. Surgical diseases of stomach and duodenum. Dr. M. G. Gillespie
11. Kidney function tests; interpretation. Dr. A. H. Wells
13. Interns' clinical-pathologic conference; case presentation. J. J. Hartford
17. Diseases of sinuses; therapeutic suggestions for general practitioner. Dr. A. C. Hilding
18. Thyroid diseases. Dr. T. O. Young
20. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
24. Practical observations on common diseases of the nervous system. Dr. L. R. Gowan
25. Employees' compensation laws and disability evaluation (case demonstrations). Dr. N. J. Braverman
27. Interns' clinical-pathologic conference; case presentation. J. J. Halbert

March 3. Most common dental disorders, also dental specialties. George Lawson, dentist
4. Foci of infection and tonsillectomy. Dr. A. G. Athens
5. Pediatric-pathologic conference, 5:15.
6. Hospital medical literature review for February. E. C. Strauss
10. Diagnostic procedures in genito-urinary tract. Dr. M. A. Nicholson
11. National, state and county medical societies. Dr. W. A. Coventry
13. Interns' clinical-pathologic conference; case presentation. E. Emerson
17. Federal, state, county and city health departments. Dr. C. A. Scherer
18. "State medicine." Dr. A. J. Spang
20. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
24. Geriatrics. Dr. E. L. Tuohy
25. Practical observations on cardiac diseases. Dr. F. J. Hirschboeck
27. Interns' clinical-pathologic conference; case presentation. William T. Cleaves
31. Useful nursing procedures for a general practitioner. C. Overley, R.N.

April 1. Management of dystocia and forceps. Dr. J. R. Manley
2. Pediatric-pathologic conference, 5:15.
3. Interns' clinical-pathologic conference; case presentation. C. Christensen
7. Gastrointestinal disturbances in children. Dr. S. N. Litman
8. Convulsive states in children. Dr. E. E. Barrett
10. Hospital medical literature review for March. E. Steiger
14. Vaccination and preventive medicine in pediatrics. Dr. C. H. Schroder
15. Otitis media, mastoiditis and the general practitioner. Dr. Archie Olson
17. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
21. Demonstrated physical therapy technic (with outlines). Miss Helen Sparling, physical therapist
22. Acute surgical conditions of the abdomen. Dr. C. H. Mead
24. Interns' clinical-pathologic conference; case presentation. W. F. Vaudreuil
28. Orthopedic problems in general practice. Dr. M. H. Tibbetts
29. Practical therapeutics (prescriptions). Dr. F. H. Magney

May 1 Interns' clinical-pathologic conference; case presentation. E. C. Strauss
5. Practical therapeutics (prescriptions). Dr. F. H. Magney
6. Allergy in office practice. Dr. C. M. Smith
7. Pediatric-pathologic conference.
8. Interns' clinical-pathologic conference; case presentation. E. Steiger
12. Venereal diseases in general practice. Dr. G. C. Doyle
13. Office hematology. Dr. P. F. Eckman
15. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
19. Practical endocrinology. Dr. M. O. Wallace
20. Functional bleeding of uterus. Dr. S. C. Mueller
22. Hospital medical literature review for April. R. R. Lannin
26. Office gynecology. Dr. M. O. Wallace
27. Home obstetrics. Dr. D. F. Pennie

June 2. Office gynecology. Dr. M. O. Wallace
3. Infections of the hand. Dr. F. J. Elias
9. Accounting, collections and income tax for physicians (with bookkeeping blanks). Mr. Richard Fox, accountant
10. Medical economics. Dr. C. M. Smith
16. Doctor's office equipment. Dr. M. O. Wallace
17. Starting in country practice. Dr. R. H. Puumala
19. Monthly clinical-pathologic conference, 7:20. Monthly hospital medical staff meeting, 8:20.
23. Doctor's medical kit. Dr. L. L. Merriman
24. Office gynecology. Dr. R. J. Moe

### The Doctor and the Community

It is time that every physician study the social and economic forces influencing the lift of his patient as well as the technical, clinical and physiologic disturbances affecting his physical and mental condition. Both react on each other. It is time that every doctor realize that he is a vital part of the community in which he lives and must play his part as a citizen in civic affairs, aiding in solving the social, economic and health problems peculiar to his particular community. If he does not do this, he should not be surprised if nonmedical persons have more influence on the health aspects of civic matters than he has. It should not be forgotten that society, not the medical profession, will ultimately determine the kind of medical service it will have. It is the duty of the medical profession to educate society so it will demand the best that medical science can offer, and this can only be done if every doctor is awakened to this larger responsibility and seizes every opportunity to enlighten both his patients and his community.—Wahl, H. R.: Community Aspects of Medicine, *J. A. Am. M. Coll.* **13**: 14 (Jan.) 1938.

# The Case of James

REGINALD FITZ, M.D.
BOSTON

James came to Boston from County Cork shortly after the Spanish War, as green a youngster as any greenhorn that ever left the shores of Ireland, finely built, with an engaging manner, a grand brogue and a sound knowledge of horseflesh. In some way he became acquainted with my father, and after Charles died and old Louis got run away with and smashed up the Ellis wagon—a unique vehicle that was inherited by my father from his teacher, Dr. Calvin Ellis—James became our coachman.

James and I grew to be close friends. The day that remains best fixed in my memory of him as typifying the kind of Irish unrespectability which always was part of his charm is the one at Prides Crossing, forty summers ago. He and I had manufactured a riding tandem, with the venerable gray Major in the lead—a dignified rascal with a docked tail, trained to kick with fury when his back was tickled behind the saddle—and Phyllis following. Phyllis was a docile, long-tailed, clumsy creature, never a saddle horse, usually of cowlike placidity, and a perpetual disappointment. She must have had a congenital heart lesion, for she never had any wind. She was out of Bess, my father's favorite in the days when the Ellis wagon would draw up at 18 Arlington Street early in the morning to take him off to the Massachusetts General Hospital, and by an unremembered sire recommended by one of his pupils in the class of 1882, Dr. Goss, of Lakeport, N. H. Dr. Goss and my father respected and amused each other, and between consultations, I suspect, were likely to swap tall yarns about trottin' horses and other things not strictly medical.

On the day I remember so well, James and I decided to put the tandem over a jump, and because Phyllis was clumsy we decided to give her a lesson. We constructed a 3 foot hurdle, which we nailed solid, and then we started, Major in the lead, Phyllis behind with me on top of her, and James with a great stick in his hand, to do whatever might be needed in the way of coaxing. Major got over all right but Phyllis misjudged, crossed her legs when she tried to take off, turned a somersault, and tossed me through what seemed at least a 15 foot arc. That wasn't the worst of it; James and I might have kept that little contretemps a secret from the family, but Major escaped and in running home plowed up my mother's flower garden. So after that there were no more tandems or riding of horses that weren't meant to be ridden.

James and I continued friends during all the years of his life; when he went into business for himself and had a cab stand and used to drive my mother and father when they dined out, later when he bought a motor car and reliably took old ladies shopping or to the symphony and young ladies to and from the debutante balls at all hours of the night, and later still, when things didn't go so well and his business melted away and he had to work as best he could, doing odd jobs here and there in garages. He was too much the sportsman to go on relief or to accept charity, and to add to his worries by now he had a wife and a child to support.

James, besides being a friend of mine, also was my first private patient. In 1909, while I was a fourth year medical student, I was called to see him, and I can never forget the pride with which I answered the call. He lived in a boarding house in the South End, a dingy place, unattractive in every way, run by a landlady with a musty smell about her like her lodgings and cross because James was ill.

It was then that he told me of a youthful indiscretion a few years back when he had gonorrhea; and now he had rheumatism, not the amateurish kind which the modern student is likely to see but the good old-fashioned variety, so painful that when I walked into his room James complained that I hurt his knees by making the floor shake. I made the necessary arrangements and stayed with him until the ambulance came to take him to the Massachusetts General Hospital.

He was there for a month. His record is of interest, for James was feverish for three weeks, with painful, swollen joints; first the knees, later the elbows and wrists. He had leukocytosis with a count which fell gradually from 20,000 to 8,000. While he was febrile his urine contained a little albumin and a few hyaline casts, but later all signs of renal irritation disappeared. He had two positive blood cultures from which grew a diplostreptococcus without a capsule, which was slightly biscuit shaped and appeared to have the morphologic and cultural characteristics of the Diplococcus rheumaticus described by Poynton and Paine.[1]

At that particular time, medical Boston was much interested in the work of these investigators. Poynton and Paine thought they had found an important cause of rheumatism, a diplococcus which grew in liquid mediums in streptococcus chains. In three cases they had

From the Robert Dawson Evans Memorial for Clinical Research and Preventive Medicine, Massachusetts Memorial Hospitals.

1. Poynton, F. J., and Paine, A.: The Etiology of Rheumatic Fever, Lancet 2:861-869 (Sept. 22) and 932-935 (Sept. 29) 1900.

isolated the organism from the blood of patients during life, but these patients, in addition to rheumatism, were suffering from acute pericarditis. They said "We cannot claim that the diplococcus is the only cause of rheumatic fever.

Fig. 1.—Appearance of James's heart in 1937 (A) and 1939 (B): The size of the cardiac silhouette is nearly identical. Why did the heart enlarge to such an extent before 1937 and not appreciably thereafter?

That it is one cause, we believe to be proved to all practical purposes." Thus the finding of this alleged organism in two blood cultures from James appeared significant, particularly because he seemed to have neither endocarditis nor pericarditis nor any other form of rheumatic heart disease. His heart was not enlarged, nothing abnormal was heard in it beyond a faint systolic murmur, and he had no cardiac symptoms. He grew better gradually, and when it became appropriate he was discharged from the hospital with the diagnosis of infectious polyarthritis.

He got along well for the next several years, prosperously, happily and healthfully. I felt embarrassed whenever I met him, for he would give me a fine reputation and volubly tell his friends that his good health was in the main attributable to my adroitness in getting him into the best hospital in Boston quickly when he was like to die of rheumatism.

In 1918 he had an attack of influenza. How serious this was is not certain, for it was during the World War and I did not see him, but at least he claimed it was as near the death of him as could be. In 1919 he married, and in the course of time his wife had a baby who died and another who lived. It was shortly after this that all the breaks seemed to turn against him. The private livery business began to fade away and he found the financial load of raising a family a heavy one. The death of his child bothered him. He had an attack of cholecystitis and had to have an operation, and this left him with a hernia. Business went from bad to worse; he became a chronic worrier, a disgruntled, unhappy pessimist, and he lost his Irish cheerfulness. Finally he began to get short of breath. In the spring of 1936 he said that he had been coughing all winter; now he was broken winded like old Phyllis, and his feet were swelling. He was glad to enter the Peter Bent Brigham Hospital for repairs.

In 1909, at the Massachusetts General Hospital, the left border of cardiac dulness was 11 cm. from the midsternal line and James's heart did not seem enlarged. Now the cardiac dulness seemed no greater and there were no murmurs. But the blood pressure was elevated to 200 systolic, 100 diastolic, and he was in bad congestive failure with fluid at both lung bases and peripheral edema.

He had an ominous-looking electrocardiographic tracing and a positive Wassermann test and Hinton test, but the urine, the renal function and the spinal fluid were normal and he responded well to treatment. Under rest in bed, digitalis and diuretics he lost 6 Kg. in weight in thirteen days and left the hospital much improved.

After his first break in cardiac compensation he got along fairly well for more than a year, taking life as easily as he could, avoiding hard physical labor, and constantly humiliated by being unable to support his family as he would like. In August 1937 he had to return to the hospital with uncomfortable shortness of breath and swollen ankles. The heart now appeared larger, though no murmurs were audible. The electrocardiographic tracing was as abnormal as ever, the blood pressure was high, the urine was normal and the renal function was not depressed. The blood serologic reaction was positive, though the spinal fluid again was normal. Once more James responded well to treatment; during three weeks of rest he lost 8 Kg. in weight, and he finally left the hospital much improved.

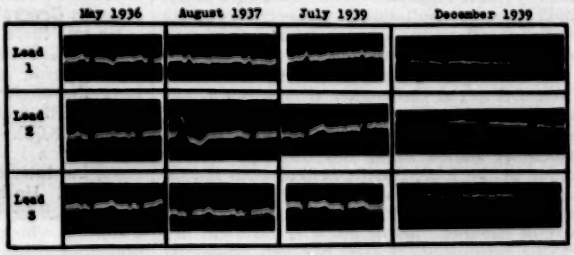



Fig. 2.—Tracings from May 1936 to December 1939: In 1936 and 1937 there were occasional extrasystoles of both auricular and ventricular origin (not shown). The electromotive force of the heart was low. $T_1$ was inverted. Auricular fibrillation was first recognized in 1939. The appearance of the ventricular complexes remained essentially unchanged.

The second break in compensation could not have been as incapacitating as the first, for

after it James had two years of comparative comfort; and in 1939, when he made his third trip to the Brigham Hospital, he said he came there not so uncomfortable as he had been previously but because he was on the way to

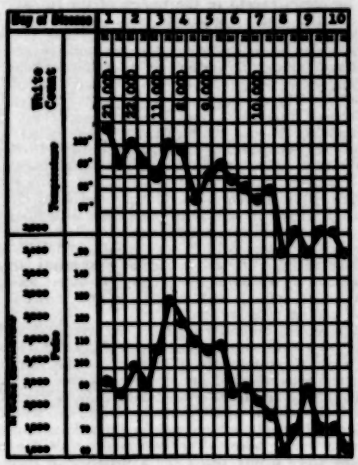



Fig. 3.—Temperature and pulse: Acute appendicitis occurred as a terminal complication of long standing congestive heart failure.

getting badly ill and experience had taught him the sense of entering a hospital early so that his stay there could be short. He had the same old complaint of increasing shortness of breath, now complicated by a sense of sternal oppression when he exerted himself.

The heart was very large, with the left border of dulness apparently 3 cm. farther from the midsternal line than it had been two years previously; the blood pressure was a trifle lower, having fallen to around 160 systolic, 100 diastolic; a moderately loud systolic murmur was audible over the precordium. The urine and renal function were normal; the Wassermann reaction had become doubtful, though the Hinton test was as definite as ever.

Two new features now were noticed. The auricles were fibrillating, but otherwise the tracing was much as it had been. During his stay a transitory attack of jaundice developed with the appearance of bile in the urine and an elevated icteric index, unassociated with cough or chest pain. This episode suggested that he might have had a small pulmonary embolus, though of this there was no definite proof. On the whole, he appeared to get along well enough and left the hospital after two weeks. Digitalis, good nursing and diuretics reduced his weight by 12 Kg. He was discharged edema free and, so far as could be told, in fairly good condition.

It soon became evident that something had occurred to make James's heart less efficient now than ever it had been before, because within a few weeks time cardiac decompensation recurred. James grew so short of breath that he was uncomfortable even at rest and, no matter how quiet he remained, edema tended to redevelop. He noticed another disturbing symptom. He suddenly began to have polydipsia and polyuria. His doctor told him that he had sugar, that he must take insulin and that he needed hospitalization.

The Brigham Hospital happened to be full at the moment but my colleague Dr. Chester Keefer was kind enough to admit James to the Evans Memorial. It was the same old story: congestive failure from a huge heart without significant murmurs and in auricular fibrillation, able to improve under bed rest, good nursing, digitalis and diuretics. On this occasion perhaps there was more evidence than previously of renal damage. The initial specimen of urine contained more albumin than heretofore, the blood nonprotein nitrogen was 45 mg. per hundred cubic centimeters, and the urinary sediment contained more casts. As the congestion cleared up, however, the albuminuria disappeared, the nonprotein nitrogen reverted toward normal and the casts disappeared, so that it seemed as if most of the renal damage was due to passive congestion rather than to any significant renal disease. The urine was found not to contain sugar, and several fasting blood sugar determinations revealed a concentration of between 120 and 140 mg. per hundred

Fig. 4.—Section through the right ventricular wall showing relatively normal coronary arteries and the diffuse nature of the myocardial fibrosis; slightly reduced from a photomicrograph with a magnification of about 25 diameters.

cubic centimeters, so that whatever diabetic tendency James had appeared to be ephemeral. The Wassermann reaction was negative, though the Hinton test was as positive as ever.

James still had a heart remarkable in its ability to recuperate from all insults. It was

notably enlarged; and while it previously produced a bad looking tracing with regular rhythm, now it continued to produce an equally bad looking tracing with fibrillation.

Yet in 1936, when compensation first broke, the circulation time was thirty-three seconds, the best vital capacity determination was 2,150 cc., and the venous pressure was 130 mm. of water. Now the circulation time was from thirty-three to forty seconds, the best vital capacity was 2,840 cc., and the venous pressure fell from 160 to 105 mm. of water under treatment. There was but little measurable evidence that his heart had grown much worse.

James's weight curve is of interest as an indicator of what his disease was doing to his general condition.

There had occurred a progressive loss in weight when he was free of edema and this, I believe, has always a significant meaning. Apparently, James was going downhill steadily in spite of whatever could be done in the way of treatment: he was drying up and withering like the leaves in the fall.

He stayed in the Evans Memorial for three weeks. He had been at home after this hospital entry for not more than a few days, when suddenly one night there developed an agonizing lower abdominal pain, unaccompanied by nausea or vomiting but preceded by slight diarrhea. He returned to the Massachusetts Memorial Hospitals at once. He had slight fever, leukocytosis and localized lower abdominal tenderness. Some observers thought that there was a tender mass to be felt in the right lower quadrant. His general condition was so poor as to make any surgical procedure unwarrantable. At first he seemed to get the best of his troubles, but later his temperature became subnormal and he sank rapidly.

Those who saw him felt that he had either acute appendicitis or thrombosis of a mesenteric vessel. To me it is a queer twist of fate that made my father's old coachman, my first patient and a man whose case I had followed for thirty years, die at the age of 62 as the result of acute appendicitis, a disease that had always so much interested his former employer.

### NECROPSY

The necropsy was performed by Dr. Charles F. Branch, of Boston University, who furnished a detailed account of his various observations:

In the region of the appendix at the lower end of the right lateral gutter, just at the pelvis brim, were several coils of small intestine firmly matted together by partially organized fibrinous adhesions. These formed the roof of a well localized pelvic abscess which contained approximately 50 cc. of thick creamy foul-smelling purulent material. The appendix was found lying in the upper lateral wall of this abscess cavity. It was approximately 6 cm. in length. Its proximal four fifths averaged 6 mm. in diameter, while its tip was distended to approximately 1 cm. in diameter. The tip was represented by a grayish green slough, from which there was a perforation into the abscess cavity. The proximal portion of the appendix showed relatively little gross pathologic change.

Microscopic examination of the appendix showed its lumen to be filled with neutrophils and the mucosa to be intact except in the region of the tip, at which point the entire appendix was represented by a sloughed gangrenous mass of tissue. The vessels of the serosa were engorged, but the smaller arterioles showed no specific pathologic alteration or occlusion.

The heart weighed 640 Gm. It was firm and contracted. The myocardium was hypertrophied and nonfriable. The right ventricle was especially large, measuring 1 cm. in thickness. There were a few small scattered areas of fibrosis to be seen throughout the muscle, none of which measured more than 5 mm. in diameter.

The right auricle was dilated, measuring approximately 10 cm. in diameter when fully distended. The right auricular appendage was occluded by an oval thrombotic mass which was firmly attached at the auricular tip. The left auricular appendage also was occluded by a similar though slightly larger mass; this was much softer and more friable and showed extensive central liquefaction.

There was no endocarditis. The tricuspid and pulmonary valves were normal except for a slight increase in their measurements. The base of the mitral and aortic cusps showed an advanced degree of arteriosclerosis. The mitral commissure showed a semilunar sclerotic plaque approximately 3 cm. in width and 1.5 cm. in depth which was in immediate apposition to the aortic base. The commissures of the aortic cusps were firmly fused for a distance of from 5 to 7 mm. and showed considerable calcification.

*Hospital Weight Measurements in the Case of James*

| *Date* | *Weight at Entry (Kg.)* | *Weight at Discharge (Kg.)* |
|---|---|---|
| May 1936..... | 88.4 | 82.4 |
| August 1937..... | 88.8 | 81.0 |
| July 1939..... | 86.5 | 74.6 |
| November 1939... | 79.5+ | 71.8 |

The coronary arteries were patent but showed numerous points of narrowing due to calcified atheromatous plaques. There were extensive stretches of coronary vessel, however, which showed no gross intimal damage.

Microscopic examination through various portions of the heart, including sections from the right and left ventricles, the interventricular septum and the auricles, all showed a peculiar fibrosis, much more noticeable microscopically than to gross examination. In general, the muscle bundles stained normally, showed their cross striations to be well preserved, and only in rare instances beneath the endocardium presented any evidence of hydropic degeneration. The increase of connective tissue throughout the myocardium presented surprisingly little pathologic change indicative of any specific cause other than that customarily associated with simple coronary occlusion. No Aschoff bodies were observed in the several sections examined. An occasional area of diffuse infiltration with small numbers of lymphocytes was the most prominent feature observed, and this was more marked beneath the pericardium than elsewhere. Here the clumps of lymphocytes tended to be arranged around blood vessels.

The arterioles throughout the heart showed varying degrees of atheromatous degeneration; however, no occlusive lesions could be demonstrated.

The aorta showed advanced atheromatous degeneration throughout its entire course, with extensive plaques of calcification in the abdominal portion.

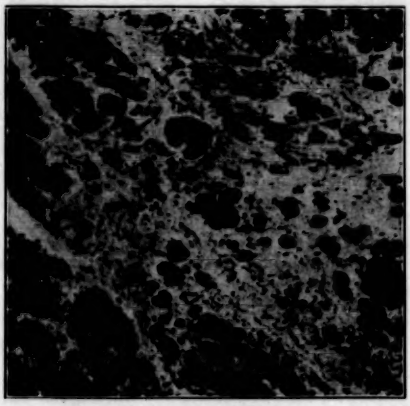


Fig. 5.—Section through the interventricular septum showing in greater detail the diffuse fibrosis; reduced from a photomicrograph with a magnification of about 250 diameters.

Many of these formed shalelike excrescences protruding into the lumen. About the margins of such lesions were typical old atheromatous ulcers. Throughout the thoracic portion of the aorta were several areas of white fibrous thickening of the intima, accompanied by many closely set linear puckerings presenting the characteristic "tree bark" appearance of syphilitic aortitis.

Microscopic examination of the thoracic aorta showed a marked fibrous and hyaline thickening of the intima beneath which were extensive deposits of atheromatous debris, cholesterol crystals and fat laden macrophages. The internal elastic membrane was badly distorted and ruptured at several points. The media showed numerous areas of scarring and many areas of perivascular fibrosis infiltrated with plasma cells and lymphocytes. The vessels of the adventitia showed similar perivascular infiltration.

The heart obviously was badly damaged by a diffuse and fairly uniform fibrosis which was not at all characteristic of healed rheumatic fever or of a possible gonococcic infection or altogether characteristic of simple arteriosclerosis. The degree of coronary sclerosis did not appear commensurate with the diffuse myocardial fibrosis at hand. The picture in the upper aorta was compatible with the diagnosis of syphilis. Dr. Branch suspects that the myocarditis was of syphilitic origin, though he is not certain. He raises another interesting suggestion: Could the diffuse myocardial fibrosis be the end result of successive bouts of interstitial edema and be due fundamentally to lack of vitamin B—an atypical beriberi heart?

The lungs were noteworthy in that the larger arteries throughout each lobe showed large numbers of soft raised atheromatous plaques which partially occluded many vessels. The degree of gross pulmonary arteriosclerosis was considerably more marked than is usual in an individual of the patient's age. No evidence of pulmonary embolism was discoverable.

On microscopic examination the bronchi were well preserved, although the musculature of the larger bronchioles was distinctly thin and atrophic. Occasional peribronchial arterioles showed edema of their walls and definite infiltration with lymphocytes and endothelial cells. The larger arterioles tended to show an edematous, myxomatous appearance of their media and adventitia, with numerous patches of atheromatous degeneration of their intima. No completely occlusive lesions were found, although many of the smaller arterioles were distinctly narrowed. In general the alveoli were either emphysematous or atelectatic, with definite diminution of elastic tissue in the interalveolar walls and containing varying numbers of hemosiderin laden macrophages. There was nothing in the picture suggestive of Ayerza's disease, nor were there any microscopic lesions compatible with the degree of arteriosclerosis noted grossly. On the whole, the histologic picture was that of long standing chronic passive congestion.

The kidneys weighed 430 Gm. On section, the normal relationship between the pyramids and the cortex was well defined, the latter measuring 8 mm. in width. The capsule stripped with some difficulty, leaving a finely granular, deeply pitted, bright reddish brown surface on which the capillary network stood out sharply. There was a moderate amount of pelvic fat. The pelvic epithelium and ureters were normal. The renal arteries showed a marked degree of arteriosclerosis throughout their entire length. There was no gross evidence of frank obstruction due to kinking or atheromatous plaques.

Sections through various portions showed certain subcapsular areas in which the glomeruli were sclerosed and the tubules were atrophic or absent and where the relative increase of connective tissue was infiltrated with small numbers of lymphocytes. In general, however, the glomeruli were in remarkably good condition, and their afferent and efferent arterioles stood out sharply as normal appearing vascular entities. The tubules were relatively normal in appearance, the epithelium being intact and the lumens containing but a small amount of amorphous coagulum. The capillaries were markedly engorged. Pathologically, the kidneys showed no marked degree of vascular nephritis: it is not remarkable that the renal function remained so normal.

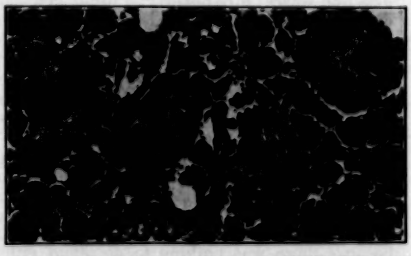


Fig. 6.—Section of pancreas; There is considerable fibrosis and hyalinization of the islands of Langerhans; reduced from a photomicrograph with a magnification of about 250 diameters.

The pancreas weighed 80 Gm. Grossly it appeared normal. Histologically the appearance was that of diabetes. There was a moderate general increase of connective tissue throughout, with moderate numbers of increased fatty trabeculae. In many places the connective tissue was infiltrated with small numbers of lymphocytes and plasma cells. The majority of the islands of Langerhans showed some degree of hyalini-

zation varying from partial replacement of one or two cords to almost complete fibrosis of the entire unit. The arterioles everywhere showed a marked fibrous and hyaline thickening of their intima, in places amounting to complete occlusion.

The ductular epithelium at occasional points showed definite evidence of metaplasia. This, Dr. Branch believes, was probably due to vitamin C deficiency.

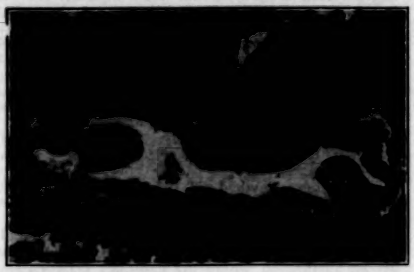


Fig. 7.—One of the pancreatic ducts showing epithelial metaplasia; reduced from a photomicrograph with a magnification of about 100 diameters.

The other organs showed no significant changes beyond such as were compatible with long standing chronic passive congestion.

## COMMENT

I have reported the case of James at length because it is interesting from many points of view. Here was a man who, during thirty years of adult living, went through a variety of vicissitudes almost entirely under the eye of one doctor: gonorrhea and unrecognized syphilis; an attack of rheumatism with positive blood culture; a period of strenuous living, including hard work and a great deal of exposure to bad weather and long hours; an attack of influenza; a major surgical operation; a period of unhappiness and worry; dire poverty; a prolonged sense of frustration because his later years were so different from what he hoped they might be. From all this chain of circumstances there developed hypertension, a badly diseased heart without clinical evidence of valvular disease, probably diabetes, surely syphilitic aortitis and much generalized arteriosclerosis.

One might argue that the necropsy in the case of James was useless, that the prognosis was plain at the time of his first decompensation, that it made no difference whether, at the end, he had mesenteric thrombosis or appendicitis, because there was nothing to do about either, and that the diagnosis was evident long before his death, clearly labeling him as being nothing more than just another cardiorenal-vascular patient.

On the other hand, cardiorenal-vascular disease is today one of the most important pathologic entities, about which very little is known. What made James have vascular disease at all? How did he escape rheumatic heart disease? How much of a part which might have been prevented did syphilis play in the illness? Why did high blood pressure develop? Why did he not have angina pectoris? Why did he escape renal insufficiency? Why did he have so striking a degree of right ventricular hypertrophy? Why did his heart hypertrophy so greatly? What made a positive Wassermann test become doubtfully positive and finally negative without any treatment? What part did other infections than syphilis play in the breakdown of his health—or hard work, or exposure to all kinds of weather, or unhappiness, or avitaminosis from faulty diet due to poverty? Why did auricular fibrillation develop and how did this affect the function of his heart? With marked pancreatic lesions supposedly characteristic of diabetes, why did not clearcut signs and symptoms of this disease develop? Why did he have appendicitis? All these questions, and many others, come to mind when the case of James is studied in its entirety.

My own idea is that such questions can never be answered satisfactorily until the life cycle of a large group of individuals like James is studied. A great many cases like that of James must be followed medically during the entire lifetime, must be examined at the end by a pathologist and must be reported in readable fashion. In due course of time, by such means, information can be assembled which may be of great importance. At present great emphasis in clinical investigation is likely to be placed

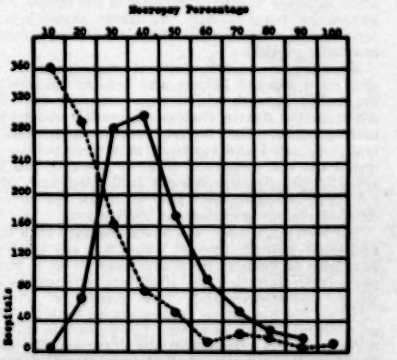



Fig. 8.—A comparison in necropsy percentage: The dotted curve represents the necropsy percentage in 556 hospitals approved for intern training in 1928 (THE JOURNAL, March 30, 1929, p. 1056). The solid curve represents the necropsy percentage in 729 hospitals approved for intern training in 1939 (ibid. Aug. 26, 1939, p. 832). To make the figures comparable, each curve has been plotted on the basis of a thousand hospitals.

on short term physiologic or chemical research and but little on the more time consuming, more elusive study of man as a whole. This is only natural because a young man at the commencement of his career wishes immediate results

with immediate publication and is unlikely to be patient at starting on a problem which he knows can never be finished during his lifetime. Hospitals, however, can do more than they now are doing to help in the accumulation of carefully documented experience regarding the life history of human disease observed over a long period of time.

A chart constructed from data published from time to time in the educational or hospital numbers of THE JOURNAL yields significant information.

Even in the hospitals approved for intern training there still is evident too much inertia regarding careful clinical and pathologic correlation. While notable progress has been made in the last thirteen years, owing largely to the efforts of the Council on Medical Education and Hospitals, the percentage of necropsies to deaths in many hospitals should be higher than it is at present. That a necropsy percentage of over 70 is possible was demonstrated last year in twenty-seven institutions, and that a remarkable general renaissance is being stimulated in the attitude of hospitals toward the importance of pathology to clinical medicine is very apparent. Those hospitals with the best records in clinical-pathologic correlation are mainly government hospitals or teaching hospitals intimately connected with medical schools. All hospitals which train interns are teaching hospitals. Each staff member of any of these hospitals must constantly remember that he is a teacher and remind himself, in his capacity as preceptor, that his interns will imitate him for the rest of their days. He must teach them in diagnosis and treatment that the complete understanding of the individual patient is of paramount importance.

The ultimate duty of a decent doctor to his patient is to bring to light discrepancies between clinical and pathologic data. It is by this method that mistakes are discovered and that important advances in the knowledge of man and his reactions to disease and environment are still to be made.

319 Longwood Avenue.

# Personal Problems and Attitudes of Medical Students

NORMAN R. FIELDER, M.A.
Program Director, West Side Professional Schools Department, Y. M. C. A.
CHICAGO

A widespread interest in this work was indicated by the responses received from the first surveys published in the Student Section of THE JOURNAL, Nov. 25, 1939, and the results of last year's clinics. Sixteen leading medical schools and several other educational institutions in different states have asked for additional information. Some have expressed a desire to cooperate further. Many practicing physicians have responded favorably.

The 1940 Medical Students Problems Clinics were characterized by the extension of the personal problems survey to include a larger number of students, the widening of the scope of the clinics to include many hitherto unsolved social and personal problems of students, and a growing interest on the part of faculty and students.

## ORIGIN OF THE CLINICS

The present clinics are an outgrowth of a project instituted three years ago by the Inter-Medical Schools Student Council of the West Side Medical Center in Chicago, following addresses by Dr. Harry A. Overstreet, head of the Department of Psychology and Philosophy of the College of the City of New York; Dr. Morris Fishbein, Editor of THE JOURNAL; Dr. David J. Davis, dean of the University of Illinois College of Medicine; Dr. T. T. Job, Loyola University School of Medicine; Dr. F. L. Lederer, University of Illinois College of Medicine; Dr. G. E. Wakerlin, University of Illinois College of Medicine; Dr. G. B. Hassin, University of Illinois College of Medicine; Dr. Arthur H. Compton, scientist, University of Chicago, and other outstanding leaders in the field of education and medical practice. Interest in personal problems of students began to crystallize. After many consultations with teachers and practitioners including Drs. H. M. Sheaff, and A. E. Diggs of Rush Medical College, Drs. William H. Welker and Bernard Fantus of the University of Illinois College of Medicine, Dr. Noyes, dean, University of Illinois Dental College, and Dr. McNulty, Chicago College of Dental Surgery, and others, the first clinics were developed. Each clinic has been under the leadership of a commission consisting of several students and one or more faculty members.

In 1940 more than 3,500 students who were enrolled in the different schools located in the Chicago area participated in the study.

This year's Medical Students Personal Problems Clinics were developed around the basic areas of student concern emerging from the experience of the past three years. The resolu-

Much credit is due to the administrations of the schools who gave permission for the studies in their institutions. Also, cooperation was shown by the many faculty members, who gave consent for students conducting the survey to appear before classes. Distribution of the questionnaire to so many people would have been impossible if it had not been for the help and teamwork of a large number of interested students who helped in the drafting of the questions. Many gave freely of their time and efforts in the circulating and collecting of returns.

tion on medical education adopted in Kansas City at the eighty-seventh annual session of the American Medical Association continued to serve as a guiding influence.

The specific problems were determined by a questionnaire and through an exhaustive analysis of student situations and personal problems. Other general problems were drawn out of the common interest and daily activities of students now engaged in attending medical schools.

Underlying the entire procedure was recognition of the requirement that the student shall be thoroughly prepared to take his place in society both as a citizen and as a skilled practitioner and community leader with the understanding and ability necessary to meet the basic problems. In brief, the fundamental problems of satisfactory living were the goals sought in the clinics.

## METHODS OF PROCEDURE

Since the field covered by this project had never been surveyed by a similar type group, it was necessary to develop most careful methods of procedure. All information received was carefully tabulated and every step checked. When the information was finally compiled it enabled the investigators to compare the latest results with the earlier observations.

From the beginning the leaders were agreed that the project should be shorn of undesirable approaches and that the methods of the clinics must be to employ the technics of the modern laboratory in an exacting examination of the personal and social problems confronting the medical student. On the assumption that individual development takes place best when efforts are directed by clear purposes and reliable information, the program was presented around those important problems determined by analysis of situations which confront every student and faculty member in the medical school.

Medical students live a strenuous life in a constantly changing world. No one is spared the struggle to make adjustments to new conditions. Disastrous social conflicts are to be found among those who cannot adjust themselves to new conditions.

Unsatisfactory living on the part of the individual is a direct result of inability to harmonize with one's environment. The task of training for the medical profession is inseparably related to the broader field of adult education and includes community activities and other social pursuits. It is an indispensable factor in advancing social and professional standards that the future medical man acquire these broader skills in conjunction with the technical professional training.

## THE QUESTIONNAIRE

To secure a proper setting for the discussions of the clinics and to provide a source of valid information, the following questionnaire was devised and used by the students:

*Please Do Not Sign Your Name!* Your help is requested in gathering information regarding what medical students do and think. The answers to the questions, when compiled, will provide a substantial basis for the discussions of the Medical Students' Problems Clinics. Please be honest. In no way will there be any attempt made to identify you with your answers.

*Q.*—Sex? *Q.*—Age? *A.*—Average 26. *Q.*—Married? Single? Divorced? School? Year? Religion? Race?

1. *Q.*—Do you feel that you personally are in need of more cultural training and background to equip you for the practice of your profession? *A.*—Yes 63%, no 37%.

2. *Q.*—Do you use alcohol? *A.*—Moderately 70%, not at all 20%, excessively 10%.

3. *Q.*—Which of the following have you attended more than three times during the school year? *A.*—Opera 3%, plays 6%, movies 25%, church 10%, concerts 9%, athletic activities 13%, read nontechnical books 12%, night clubs 9%, taverns 9%, burlesque shows 1%, gambling "joints" 2%, lectures (not required).

4. *Q.*—How do you prefer to attend these? *A.*—Alone 14%, with your own sex 30%, with the opposite sex 56%.

5. *Q.*—Do you have a college degree? *A.*—Yes 65%, no 35%.

6. *Q.*—Do you intend to specialize in a branch of your profession which requires further study after you have completed your present course? *A.*—Yes 53%, no 47%.

7. *Q.*—Roughly what percentage of your courses do you consider time wasted? *A.*—25%.

8. *Q.*—Does the curriculum leave you enough time for social interaction and enough leisure to pursue other interests? *A.*—Yes 59%, no 41%.

9. *Q.*—Roughly what percentage of your instructors do you consider good teachers? *A.*—50%.

10. *Q.*—Do you depend on religion for personal satisfaction? *A.*—Yes 37%, no 63%.

11. *Q.*—How do you attend church or religious meetings? *A.*—Regularly 7%, occasionally 10%, never 83%. *Q.*—If you do not attend regularly, why? *A.*—Work 10%, sleep 75%, indifference 15%, fear of ridicule 0.

12. *Q.*—Since entering professional training, how has your regard changed toward the church? *A.*—Greater belief 30%, less belief 70%.

13. *Q.*—Regardless of financial status of the student at what time during his training is marriage advisable? *A.*—First two years 18%, last two years 25%, internship 27%, "starvation period" 30%.

14. *Q.*—Compared with your intellectual level, what sort of person would you prefer to marry? *A.*—Below 0%, even with 74%, above 26%.

15. *Q.*—Do you approve of women physicians? *A.*—Yes 27%, no 73%. *Q.*—If any of your family were ill, would you call a woman physician? *A.*—Yes 38%, no 62%.

16. *Q.*—Do you approve of girls sharing expenses on dates? *A.*—Yes 76%, no 24%.

17. *Q.*—In a word, what do you regard as the most undesirable characteristic in students of your school? *A.*—First selfishness, second egotism, third rudeness, fourth cheating.

18. *Q.*—Have you ever had a venereal disease? *A.*—Yes 3%, no 97%. *Q.*—Indulged in sexual intercourse before marriage? *A.*—Yes 60%, no 40%. *Q.*—Indulged in sexual intercourse when engaged? *A.*—Yes 72%, no 28%.

19. *Q.*—Do you use contraceptives personally? *A.*—Yes 85%, no 15%. *Q.*—Do you favor their use by the lay public? *A.*—Yes 89%, no 11%. *Q.*—Do you think the doctor should be trained to give this information? *A.*—Yes 97%, no 3%.

20. *Q.*—Where do you plan to practice? *A.*—In a large city 79%, small community 21%.

21. *Q.*—How is your physical condition and health as compared to how it was when you entered the professional school? *A.*—Same 65%, worse 35%.

22. *Q.*—Have your moral attitudes changed since being in training? *A.*—More critical 27%, more lax 73%.

23. *Q.*—Do you understand the Wagner bill? *A.*—Yes 46%, no 54%.

24. *Q.*—If the United States declared war for any reason would you volunteer for military service? *A.*—Yes 25%, no 75%.

25. *Q.*—Are the students in dentistry, medicine, pharmacy and nursing professions more careless than the average in dress? *A.*—Yes 57%, no 43%.

26. *Q.*—Is a professional student justified in accepting financial support from his wife? *A.*—Yes 72%, no 28%.

27. *Q.*—Do you feel that your profession has hardened you to human need? *A.*—Yes 36%, no 64%.

28. *Q.*—Do you favor some college training for admission to nursing school? *A.*—Yes 100%. *Q.*—If so, how many years? *A.*—Average two years. *Q.*—To medical school? *A.*—Average three years. *Q.*—To dental school? *A.*—Two years. *Q.*—To pharmacy school? *A.*—Two years.

29. *Q.*—During your professional training how has your belief in a personal god become? *A.*—More important 32%, less important 68%.

30. *Q.*—Do you consider your professional school colleagues adequately schooled in etiquette? *A.*—Yes 40%, no 60%.

31. *Q.*—Do you feel that your professional training tends to make you humble? *A.*—Yes 30%, no 70%.

32. *Q.*—Are you influenced by propaganda? *A.*—Yes 54%, no 46%.

33. *Q.*—Do you believe in regimentation of your profession? *A.*—Yes 3%, no 97%.

34. *Q.*—Do you favor your school establishing certain standards for living conditions? *A.*—Yes 52%, no 48%.

The results of this clinical analysis show trends of thought and points of view growing out of a sincere attempt by students to face their personal problems.

COMMENT ON QUESTIONS

Questions 1, 3, 25 and 30: Investigation of these questions reveals that many cultural interests are suffering from anemia among medical students. Many an eminent educator, scientist and medical leader, brought to the field by the various schools, addresses a distressingly small audience. Recitals and concerts in the neighborhood institutions are usually attended by a small number. Neighborhood movies featuring love thrillers boast the best attendance of any institution in the whole area. In the field of current reading it is interesting to note that students buy fifty copies of *Esquire*, *True Romance* and *Detective Stories* to one copy of the *Atlantic* or *Harper's*. The only places where students go *en masse* are to required class lectures, clinical demonstrations, the movies and dances. As a matter of fact, the average medical student is not concerned with the cultural aspects of the usual uplift program planned for him. And naturally so! The medical school is a world of physical facts, clinics, dissecting rooms, microscopes, test tubes, case histories, examinations and books.

Question 8: This question seemed to include more than the curriculum—the whole scope of the daily activities seemed to be involved. Careful examination of student life inevitably takes one outside the walls of the institution responsible for the formal technical training program. Here we find that certain aspects of our twentieth century civilization draw students away from that phase of life usually called intellectual and religious. The speed of life, with radios, newspapers, crowded schedules, restlessness, fast moving crowds hurrying to go no place, all tend to induce hastiness in mental activities, which in turn breeds superficiality. With little chance to concentrate on any single field of thought, students tend to jump from one interest to another.

Question 11: Religion, as a subject for serious intellectual concern, is not popular among the great majority. It is rarely a subject for serious study and the students are conspicuously absent from services of worship conducted by churches within the community. Attendance at church services both regularly and occasionally is participated in by only 17 per cent. A breakdown of the 17 per cent attendance figure opens the way to many interesting speculations concerning the carry over results of early childhood training methods practiced by the various faiths and denominations. Of those reported as regular or occasional church attendants the nonmember of any church group ranked first with 7 per cent. Strange as this appears, on careful study it seems to substantiate the often repeated statement of students that early church going experiences, when reviewed during their professional training period, appear unattractive and unsatisfying for the scientifically trained mind. Of the remaining group, Lutherans come second with 5 per cent, Catholic students were third with 3 per cent, Baptist and Jewish come fourth and Methodists last. A fact of tremendous importance growing out of this phase of the study is that the church has not yet found a way to attract and to hold the large body of highly trained young men and women who will become our influential professional leaders of tomorrow. Can the church build a program that will grip the interest and command the loyalties of these youth?

Questions 10 and 12: One of the most interesting facts revealed by the study of these questions is that the students of all different faiths are proportionately indifferent to the church. There seems to be no doubt about it. The church for most of the students is simply not counted. It is true that some talk about it, but much as if it were a dead thing. "Jam sessions" turn to it occasionally, but their talk for the most part lacks genuine interest.

Question 18: It is recognized that there are grave dangers in premarital sexual intercourse. The social attitudes and restrictions at this point are so strong that they may be reflected in the attitudes of the two toward themselves and toward each other, even though intellectually they believe that their action is quite proper. Unintended pregnancy is a further possible source of complication. For some it is well to make a distinction between gratification and satisfaction. By gratification is meant the gaining of temporary pleasurable sensations. By satisfaction is meant the achievement, in addition to gratification, of friendship, love, beauty and all those distinctively human values which make life worth while. Certain types of sex gratifications which relieve tension and give pleasurable sensations at the time do not satisfy the complex, interrelated needs of a civilized man or woman. It is of first importance to discover how to handle sex desires so as not only to gratify but also to satisfy a cultivated person.

Question 21: It is now generally recognized that tuberculosis constitutes the main occupational hazard of the medical student. This danger is probably increased for students who are forced to work their way through the professional school. Rest with proper exercise and adequate recreation are absolute essentials in the life of students. The administrations of the schools are increasingly developing greater means of safeguarding the health of the student.

Question 22: This attempt to look facts in the face possibly has brought to some the conclusion that it's hopeless, that nothing much

can be accomplished in changing student moral attitudes for the better; medical students will go on being what they are and we cannot improve them. Such conclusions might be justified if we continue to follow the paths of old. Careful study of the customary practices of the past and the accompanying failures to make progress bring to light the fact that most of the basic principles in sound education and the essential conditions for proper cultural development have been grossly ignored. Medical students resent pressure. "Religion is my own business" is the usual reply when an overzealous worker speaks of spiritual matters.

Question 29: The results of an earlier survey were compared with the recent results, and it is significant to note that 98 per cent of the freshmen believe in God while 53 per cent of the seniors indicate disbelief in God. If these statistics indicate what takes place among students in general, it would appear that the concept of God gained by many in early youth cannot stand up under the microscopic test of a scientific training for a profession.

Question 29: It is the sincere belief of those interested in the final results of this study that the only work that promises anything worth while in the developing of personality and influencing character with medical students must be based on the spirit of science at its best, which means the uncommercialized love of truth no matter where it leads, sincere effort and eager curiosity, readiness to discard yesterday's theories in the face of newly acquired information, endless explorations built on an unquestioned belief in life.

## CONCLUSION

Leaders in the medical profession more and more are stressing the fact that the task of the physician is the most intimate and delicate in the field of public service. As soon as the student really grasps the significance of this fact he will begin to see that his professional training of necessity must include and strive to develop the social and cultural aspects of human relations.

From the view of the faculty and administrations of the training institutions the selection of prospective students will increasingly be based on more than scholastic standing, as indicated by the following resolution at the Eighty-Seventh annual session of the American Medical Association:

WHEREAS, The relationship between physician and patient embodies many factors that must be considered in the determination of an individual's fitness to be a doctor of medicine; and

WHEREAS, The entrance requirements to the degree of Doctor of Medicine cannot be evaluated on a strictly academic basis; therefore be it

*Resolved*, That the following factors be considered in the selection of students who are to become doctors: character, personality, social fitness, adaptability and motivations.

Gradually the medical schools are providing new opportunities for progressive enhancement and development of personalities of students to go along with the study of anatomy, physiology, chemistry and surgery. To prove the necessity of correlating those qualities included in the American Medical Association resolution—motivation, adaptability, social fitness, character and personality—with the technical and professional knowledge, place that physician beside the beds of sick human beings, where he must deal as much with human nature as he does with medical and professional technics. Thus it would seem that a prerequisite to graduation from a medical school would be a properly balanced personality.

How can we test the personality of a student to find whether he has the characteristics desirable in a practitioner? How are we to apply tests to determine whether a student is socially fit for the profession? These questions have been discussed in the clinic sessions by students from the various schools. The results of the questionnaire were used as a foundation.

It was agreed that one of the best ways to test each applicant for entrance to a medical school would be to find out what he has been in the past several years. Ask teachers in high school and the undergraduate colleges to keep records of students. Following are some questions that might provide essential information:

*Personality.*—1. What sort of a mask does he wear?

2. Does he mingle easily with his fellows?

3. Does he have many friends?

4. Has he any traits that make a student unable to get along with his associates?

5. Is he conceited?

6. Is he unclean in personal habits?

7. Is he undependable?

8. Is he excessively stubborn?

9. Is he quarrelsome?

*Social Fitness.*—1. Is he able to get along with others or is he cantankerous?

2. Is he upright or is he underhanded?

3. Does he have control of his emotions or is he uncontrolled?

*Character.*—1. Is he honest?

2. Has he ever been found guilty of any dishonesty?

*Adaptability.*—1. Has he traits which make him effective among his associates?

2. Has he held class positions?

3. Has he shown social snobbishness?

4. Has he been a decided recluse?

5. To what extent has he taken part in social activities?

*Recreation.*—1. Is he active in sports?

2. Does he take active part in recreations?

3. Does he sit back and observe rather than participate?

*Motivations.*—1. Was his motive in entering professional schools: (*a*) Prestige? (*b*) Egocentric? (*c*) Easy way to make money? (*d*) Sense of human service? (*e*) Having something grand to do?

2. Has he shown an interest in something other than grades?

3. Does he go out of his way to do things for others?

4. Does he devote time and interest to others than himself?

1804 West Congress Street.

## Comments and Reviews

### A MEDICAL CENTENNIAL OUTLOOK

*Condensation of an address by Dr. James Ewing, New York, delivered at the one hundredth anniversary of Albany Medical College, June 12, 1939, and published in Albany Medical Annals, December 1939.*

Centennial celebrations of medical schools are rare opportunities when we may review the long past, trace the forces which have directed the fortunes of the institution, acknowledge our debt to the several generations of strong men who have served their alma mater, and renew our allegiance to the traditions which experience has proved to be sound. The present occasion is especially notable because Union University and the Albany Medical School have a distinctive local significance and belong to that group of institutions which are peculiar to our American educational system, the smaller colleges.

Many educators think they detect in the smaller colleges certain advantages and refinements which it is difficult to preserve in the highest degree in the great universities. They seem to consist in the comparative simplicity of college life, the more friendly contacts between students and the more intimate relations with teachers. One must suspect that the smaller college is able to respect established traditions and not to yield so readily to passing popular demand for untried innovations. High scholarship, mental discipline and character building are delicate plants easily crowded out by the influx of more modern and more practical pursuits. The college graduate from the great universities is probably better fitted to make his way in the world, but the man from the small college often seems to have deeper roots and is designed to go further, at least in certain worthy directions. There is every reason to urge that the smaller colleges should maintain their unique position in our educational scheme, for many regard them as the beauty spots of our intellectual world.

#### CULTURAL VALUE OF MEDICAL STUDY

Medicine is still the mother of the sciences. Contact with the medical sciences has a powerful and a peculiar cultural influence not shared by any other intellectual pursuit. Every university needs a medical school to lend earnestness and incentive to the pursuit of pure science and higher learning. It is the significant nature of medical knowledge and its intimate relation to human values that lends to the study of medicine its peculiar cultural value. The study of medicine enables a man to follow Agassiz's advice "Know thyself." Without that knowledge it must be questioned whether any man can consider himself really educated. There is an astonishing naiveté regarding the conceptions of the average educated lawyer, clergyman and business man, not to mention the general public, about his bodily sensations and functions, his position in the biologic world, in fact his true significance as an individual, and this ignorance colors his judgments in many of the relations of life. The ancient mysticism about medicine still prevails and the medicine man still circulates freely in polite society. In a medically educated public the medical cults would not thrive. In the medical sciences the penalties visited on the adventurer and false prophet are drastic and destructive, but when medicine becomes mixed with politics the medical politician may survive several false projects merely by repeating them on a larger scale at the expense of the taxpayer, but only because there is no informed body of public opinion. There is a great need of expansion of elementary medical knowledge with the general public and of that culture and balanced judgment which goes with such knowledge, and the pervading influence of the medical department of the universities seems to be the sole source of such help.

#### FORESIGHT OF THE FOUNDERS

The history of Albany Medical College reveals a unique record of farsighted vision and heroic devotion on the part of its founders. Dr. Alden March came to Albany from Massachusetts in 1820, when the city had 15,000 inhabitants, and started a course in anatomy with fourteen students. In 1825 he was appointed professor of anatomy in the Vermont Academy of Medicine at Castleton, where he remained until 1830, when his Albany class had grown to thirty students. In 1831 Dr. James H. Armsby joined him in Albany and the two physicians worked together to found a medical college. They gave public anatomic demonstrations to a selected

group of laymen and they secured the solid support of influential citizens, who contributed the first funds for the founding of a medical school. This was a very early period in the growth of public medical intelligence for physicians to submit their interests to a group of laymen.

It has often been said that every successful pioneer institution is but the shadow of some man. In this instance that man was Dr. Alden March. In Philadelphia it was Dr. William Shippen. In Boston it was Dr. John Warren and, at Dartmouth, Dr. Nathan Smith.

Another versatile figure, Dr. James H. Armsby, joined with Dr. March in his early efforts and seems to have contributed essentially to their success. Dr. Armsby had a remarkable gift for enlisting the support of the public and in obtaining money for the school. His interests were wide, including no less a project than the founding of a well rounded university in the city of Albany.

### FORECASTING THE FUTURE FROM THE PAST

Looking backward, we are privileged to acknowledge the debt which Albany Medical College and the city of Albany owe to these strong men. What does this centennial retrospect teach for the future of medicine?

The great achievement of the past century has been the virtual control of infectious diseases and, as a result, the average expectation of life has been increased about twenty-five years and the age composition of the population correspondingly raised. Recently this line of progress has been greatly forwarded and consolidated by the discovery of chemical agents which seem able to control to a large extent the ravages of the two most formidable bacterial causes of disease, the streptococcus and the pneumococcus. It seems reasonable to expect that these epoch making discoveries in chemotherapy may be extended even further and as a result that medicine in the future will be forced to turn its main attention to the nutritional and degenerative diseases, including especially mental deterioration, cardiorenal disease, cancer and diabetes. Thus medical problems of the future loom quite as large and appear far more complex than those which occupied physicians a hundred years ago.

### A MENACE TO MEDICINE

Political and economic problems face the medicine of the future as never before in its history. Political and economic changes have radically altered the complexion of German medicine, which is not likely to regain the zenith reached about the beginning of this century. Somewhat similar limitations are beginning to appear in other European countries, and it is not safe to assume that America is immune to such forces. With us the danger lies in the lack of understanding between the public and the medical profession. The public does not and apparently can not understand the implications of disease, the vast scope and variety of bodily disorder, and the limitations of curative medicine. I believe that the lack of mutual understanding between the public and the medical profession is greater today than it was thirty years ago. The causes seem to be traceable to the greater control of curable infectious diseases and many minor disorders, and the greater incidence of the more chronic incurable diseases, for which the individual himself is mainly responsible. An important factor is also found in the decline of public morals and the sense of individual responsibility and self help. When great masses of people receive the dole, it is an easy way to assume that some one can hand out relief from disease in the same lavish manner as the government hands out money. The American public will sometime learn that it is a long way from easy money to freedom from disease. Yet certain medical authorities, some occupying positions of importance, chiefly in institutions, but not very familiar with the conditions of medical practice, not overmindful of the social significance of disease and wholly neglectful of the weakness of human nature, have assumed that by the expenditure of vast sums of money it will be possible to improve greatly the care of the sick poor and largely meet the demands of the public. The great majority of thoughtful physicians regard this project as chimerical and some, myself among them, regard it as a grave menace to the future of American medicine.

The idea that this vast sum administered by men and women who mostly lack a record of practical achievement, but are animated by the naive spirit of the big brother, can be wisely expended in a relatively brief time is unreasonable. The scheme is a utopian project designed for an ideal community. It may be suggested that in an ideal community such need would not exist. Among the many hazards inherent in this scheme, one may refer merely to the fact that the withdrawal of such a vast sum from the taxpayers will seriously aggravate the present decline in the resources of American universities and transfer to a group of relatively inexperienced governmental bureaus virtual control of the most vital and individualistic factor in modern society, the university spirit. It is to be hoped that before the federal government actually embarks on such a comprehensive and irreversible program a truce should be called of at least ten years, during which the exceedingly complex ramifications of the scheme can be analyzed by competent experts. One need not subsidize genius and one may not buy the cardinal virtues in the market place. What American medicine needs most is to be

let alone, to continue the remarkable progress of the past half century which has made medical service and research in this country equal or superior to that in any other nation, to conserve its material resources which have been poured out lavishly and intelligently by public spirited citizens, and to solve its problems methodically according to the judgment and decisions of its tried and trusted leaders. There are, throughout this country, a great number of highly competent physicians and long established medical organizations which are intimately familiar with medical problems and are dealing with them by methods tested by experience, with notable success and as rapidly as may be. Why should we transfer these multitudinous and highly technical responsibilities to a new group of relatively inexperienced persons who are far removed from the scene of action?

### NEED OF EDUCATING THE PUBLIC

To forestall precipitate action by runaway political forces it will become necessary for the medical profession to undertake a systematic program of public education, pointing out the high standard of medical service in this country, the diversion of large masses of people from private hospitals to public institutions owing to artificial economic dislocations, the growing abuse of public hospitals by tired folk and malingerers, the demoralizing influence of free medical care, the necessity of personal responsibility for personal hygiene and the avoidance of disease, the ignorance of the public in seeking medical advice, and the utter futility by any conceivable program of relieving the symptoms of innumerable minor ailments or preventing death from major lethal diseases and, above all, the vast difference between useful and noxious therapeutics. For these are days when every one seems to have his own pet ideas about major problems, and the expert must prove that he is an expert by repeated argument and demonstration. A hundred years ago, Albany doctors by public demonstration convinced the public that organized medicine can still be trusted to direct progress in its own field.

### UNRESTRAINED BIOLOGIC FORCES

Finally, political and economic movements now gathering momentum in many parts of the world promise to place on medicine of the future grave problems which it alone seems capable of meeting. The greatly increased tenure of life, the elimination of decimating epidemics, the enormous overproduction of foodstuffs and unrestrained reproductive fertility have made it possible for many more people to live on the earth, and in certain regions these biologic forces have brought about extreme overcrowding of the population. In some countries with national ambitions, these factors have been exaggerated by bonuses for large families and penalties for celibacy, so that the effect of natural biologic influences have been deliberately intensified by human ingenuity. The result has been that these nations must either burst their boundaries or limit their excess population. They have chosen the former course and have frankly adopted the doctrine that henceforth biologic forces unrestrained by human intelligence shall rule the fate of nations. The inevitable result is war. The stronger must destroy the weaker. Among the lower animals nature has provided a convenient mechanism by which the stronger species devour the weaker, or natural limitations of life or deficiency of food or slight climatic changes often erase overpopulous species. No such limiting agencies apply to the human species. We have the advantage of highly developed intelligence and a rather effective control of our physical environment. The problem of overpopulation, undernourishment and unemployment is worldwide and increasing, and it is a biologic problem not to be met by peace conferences, truces, doles, public works and taxes. Neither can it be met by praying for peace or by denouncing the nations that go to war under existing conditions. It can be met only by accepting the biologic doctrine but directing it through enlightened intelligence. The human race need not submit to the natural forces that breed and destroy the lower animals. In America we have flattered ourselves that we are not suffering from these same conditions, that we are not forcing overpopulation and have not adopted the simple biologic doctrine, but is it not clear that during the recent period of expansion many more people came into existence in this country than can be comfortably supported and that jobs for everybody cannot be artificially created? In our approach to the totalitarian state are we also not attempting to solve a biologic problem by economic measures?

### REMEDIAL MEASURES

Medicine is the instrument through which remedial measures conceived in the light of biologic principles can be made effective in relieving the present dilemma of the overpopulated nations. The medicine of the future will surely be called on to use all its resources to meet this problem, if it is to be solved at all. Rather than call a peace congress, a conference of biologists, physicians, churchmen and social economists should be assembled to find ways and means. Already many voices have urged the pressing necessity of establishing safe methods of birth control. Modern eugenics offers the possibility of a vast improvement in the quality of the race, for today a large proportion of living persons are unfit physically and mentally, as a result of hereditary and environmental factors. Since the problem is of national

scope, the federal government could aid in formulating public opinion by establishing a bureau devoted to the express object of improving the quality of the North American race. I venture to think that this task is a more essential function of government than are excursions into the field of curative medicine. The chief responsibility and opportunity probably lie with the university medical schools. As practical steps toward this end the medical schools of the future must stress preventive medicine, the science of nutrition, genetics, practical eugenics, antepartum service, endocrinology and all those branches of science which tend to place us in command of those irresistible biologic forces which determine the quality of mankind. They must cordially accept the biologic doctrine but realize that biologic forces may be modified and controlled in accordance with the dictates of the enlightened conscience. Cooperation with other departments of the university will be required to prepare public opinion to accept the conclusions and adopt the program suggested by medicine, and in this field sociology, economics and philosophy will find new opportunities and incentive.

# Medical College News

*Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items to be considered for publication in the Student Section.*

### Harvard Students After Fifteen Years

The class of 1925 of Harvard Medical School will hold a reunion in New York City, June 11, during the time of the annual meeting of the American Medical Association. Anticipating this event, Dr. William N. Wishard obtained interesting information from 100 of the 117 living members of the class. Five of the remainder live in foreign countries. The addresses of two are unknown. This class spent, on an average, three years in hospital training before assuming the actual practice of medicine; thirty-five members of the class had four years or more of training in a hospital, eighteen had five years or more and eight members had six years or more. Now at least eighty-eight members are on one or more hospital staffs. Thirty-six members answered the question about their own publications, and they had to their credit an average of 11.3 papers, monographs or books per member. Ninety-three belonged to the local and state societies and American Medical Association, three have been president of their local or state medical societies, fifty-eight are diplomates of the National Board of Medical Examiners, five are in the service of the United States. The members belong on the average to 2.8 scientific societies; two of them belong to ten and one actually to fourteen scientific organizations. Their ability to pay so many dues is explained by the fact that the average income of the members of the class was $7,000 with a maximum of $20,000 and a minimum of $3,000. One member has been appointed ambassador to an important country which is much in the limelight during these troublous days. Five members are unmarried, and fifteen of the ninety-five married members have no children. One hundred and eighty-one children have followed the eighty marriages, an average of 2.6 per couple; forty-three of them have two children, eighteen have three, six have four, and one has five children. None of the class have left the profession, one has become a full professor, nine associate or assistant professors, thirty-five instructors, and one is a hospital superintendent. Thirty-five of the hundred have gone into surgery, twenty-one into internal medicine, fifteen into general practice, nine into obstetrics and gynecology, seven into pediatrics, two are secretaries of state boards of health, and two each have gone into ophthalmology and orthopedics. Forty-five of the hundred members returned to practice in the communities from which they came to medical school.

### Scholarships Announced by Michigan Galens

The Galens, an honorary medical society, has contributed a scholarship fund of $2,000 to be awarded annually to students in the University of Michigan Medical School, at Ann Arbor, the money to come from the Galens news stand in the University Hospital. The total sum will be used to form individual scholarships, not one of which is to exceed $400. The number and size of the scholarships will be determined by the scholarship committee of the medical school, which will award the grants on the basis of the following qualifications: Recipients must be native-born citizens of the United States, must be juniors or seniors in good standing, must have completed two full years of work in the local medical school and must be enrolled at the time the grant is made. Preference will be given to students whose scholastic work in the opinion of the committee will be improved by financial aid.

### Tulane's History of Medicine Society

Thirty-five students at the Tulane University of Louisiana School of Medicine, New Orleans, have been named members in the History of Medicine Society, an honorary organization founded at Tulane in 1933, the purpose of which is to foster scholarship and interest in the history of medicine and to maintain the finer traditions of the humanities in medicine. The officers elected for the coming year are Rudolph Matas Landry '42, president; Lee Roy Murphree '42, vice president; Charles M. Wilson Jr. '42, corresponding secretary; Julian Wiener '42, recording secretary; Walter Jacques Trautman Jr. '43, treasurer, and Dr. B. Bernard Weinstein, faculty adviser.

### Georgia Faculty-Student Get-Together

The dean of the University of Georgia School of Medicine, Augusta, Dr. G. Lombard Kelly, proclaimed May 11-18 as Faculty-Student Get-Together Week. An auld lang syne dance was held Saturday evening in the former college auditorium, which faculty members and their wives attended. The regular meeting of the Faculty-Student Council was held Monday evening at the home of Dr. Peter B. Wright. Exercises were held Friday evening in the Dugas Auditorium, following which refreshments were served in the Physiology and Pharmacology Laboratory. The Faculty-Student Council was promulgated during the present year for round table discussions of faculty-student problems. Five members of the faculty were selected by the stu-

dent body to serve with nine students, two selected by each class, and the president of the student body. ——The University System of Georgia Council, consisting of the heads, deans and many teachers in the different parts of the system to the number of more than 100, was the guest of the school of medicine April 26-28.

A students' activities fee of $5, collected for the first time this year, has paid all students' hospital bills to date and has paid for two table tennis sets, two pool tables, and one badminton court and equipment.

### Annual Lecture at Louisville

The annual Alpha Omega Alpha lecture at the University of Louisville School of Medicine, Louisville, Ky., was held at the Louisville City Hospital, April 19. Dr. John A. Bigler, assistant professor of pediatrics, Northwestern University Medical School, Chicago, spoke on "The Blood Titer of Diphtheria and Tetanus Antitoxin." Sixty-six guests attended the banquet. Dr. Lee Palmer was toastmaster. The speakers were Dr. Bigler and the two graduate members-elect, Drs. Emmet F. Horine and James H. Pritchett.

### Seniors Give Notes for $200 Each

The senior class of the George Washington University School of Medicine, Washington, D. C., has unanimously presented the school of medicine with a $10,000 endowment fund, each student in the class having signed a noninterest bearing note for $200.

### Vitamin Patents to Provide Chemistry Fellowships

Lee I. Smith, Ph.D., head of the division of organic chemistry, University of Minnesota, Minneapolis, has donated to the university his 25 per cent share in the proceeds from manufacture and sale of vitamin E products under patents applied for as a result of his research, and the university has accepted the gift. It was specified that if and when the income is sufficient from the patents four $750 fellowships in chemistry be established to be awarded annually to superior students. If more than that amount of money accrues the remainder shall go to establish the Lee Irvin Smith Fund, the income of which shall be used to pay the fellowships when the patents expire.

### An Opportunity to Sing in New York

The Doctor's Choral Society, New York City, is open to medical and dental students who have vocal talent and desire to sing and who will promise steady attendance. Rehearsals are held at the studio of Maestro Alberti at the Hotel Ansonia, Broadway and Seventy-Third Street, Wednesday evenings.

### Prizes Awarded to Interns

Dr. William J. Kerr, professor of medicine, University of California Medical School, San Francisco, announced April 6 the award of the Woodward Prizes in internal medicine. Frederick S. Howard, San Jose, now an intern at the University of California Hospital, won the first prize of $150 for his paper on "Snake Venoms in Therapy—A Review of the Literature"; Melvin Friedman, Los Angeles, now an intern at the San Francisco Hospital, won the second prize for his paper on "Early Diagnosis of Gastric Neoplasms," and Arseny K. Hrenoff, San Francisco, won the third prize for his study of epidemic influenza of 1918-1919 in San Francisco. Sidney Rosin of Los Angeles and Emile J. Gough Jr. of San Francisco were given honorable mention.

### National Board Questions in Medicine

Following are the questions used by the National Board of Medical Examiners in medicine in part II of the examination held February 12-14: (Part II of the examination is given immediately after graduation from medical school.)

Answer questions 1 and 2 and three of the remaining four:

1. Discuss the principles of the diagnosis and treatment of acute poliomyelitis.
2. What pathologic conditions in the chest may produce symptoms in the abdomen? Indicate briefly differential diagnosis.
3. What disorders of the clotting and bleeding mechanisms may occur in hemophilia, scurvy, jaundice and essential thrombocytopenic purpura?
4. What disturbances in metabolism (exclusive of basal metabolic rate) may be expected in thyrotoxicosis?
5. Enumerate the diagnostic features of the history, physical examination and laboratory data that are necessary to treat adequately a case of lobar pneumonia.
6. Discuss the diagnosis and treatment of Addison's disease.

### Duke University

Dr. Halbert L. Dunn, of the U. S. Census Bureau, Washington, D. C., lectured on vital statistics before the students of Duke University School of Medicine, Durham, N. C., March 13; on the previous day, Dr. Mark V. Ziegler, U. S. Public Health Service, lectured on "Opportunities in the United States Public Health Service." "Problems of a Young Doctor in Private Practice" was the subject of an informal discussion in the Duke Hospital amphitheater, February 26, sponsored by the Nu Sigma Nu fraternity, in which questions of ethics and of the legal, social and business aspects of medical practice were discussed by Dr. Wingate M. Johnson, editor of the *North Carolina Medical Journal;* Douglas B. Maggs, of the Duke University Law School, Harold D. Meyer, sociologist of the University of North Carolina; Leroy Lewis, instructor in public speaking at Duke University, and Dr. Wilburt C. Davison, dean of Duke University School of Medicine.

### Loan Funds at the University of Pennsylvania

Information about loan funds and noncompetitive scholarships available at the University of Pennsylvania School of Medicine may be had by writing to the director of scholarships and student finances, University of Pennsylvania, Philadelphia.

Among the prizes to be awarded in June 1940 at the medical school is the Dr. Spencer Morris Prize, comprising the annual income from the investment of $28,000. The award is made to the senior medical student who shall pass the best examination for the degree of Doctor of Medicine. Among the other prizes is the Alumni Medal and a prize of $50 awarded to the member of the graduating class who attains the highest general average in examinations.

### Undergraduate Medical Association

The Undergraduate Medical Association of the University of Pennsylvania held its thirty-second annual meeting April 18. Students who have not yet received their M.D. degrees presented eleven papers. Addresses were given by Dr. James B. Collip, Gilman Cheney professor of biochemistry, McGill University Faculty of Medicine, Montreal, on "Pituitary Hormones in the Light of Recent Experimental Studies," by E. A. Singer Jr., Ph.D., on "Beyond Mechanism and Vitalism" and by Dr. Samuel C. Harvey on "The Scientific Method in Clinical Surgery." Dr. Edward S. Thorpe Jr. presented the prizes. The Mary Ellis Bell Prize was won by student Renato A. Ricca '40, the John G. Clarke Prize by student Seymour S. Kety '40, and the Grahye

Simpson Priestly Prize by student Martin G. Netsky '43. Honorable mention was given to student William H. Crosby Jr. '40.

### Loan Funds at Wisconsin

The income on $5,000 bequeathed to the University of Wisconsin by Mrs. Cora R. Evans is available as a loan fund to students in the medical school. Interest is charged at the rate of 5 per cent. Loans are made on recommendations of the dean of the medical school. There is an annual prize of $25 established by the local chapter of Phi Delta Epsilon fraternity, which is awarded at the beginning of the second year to the student who is judged to have done the best work in gross anatomy in the previous year. The university also has a number of fellowships and scholarships available under certain conditions, about which information can be obtained from the dean of the University of Wisconsin Medical School, Madison.

### Alumni-Senior Picnic

At the annual picnic of the senior class of the College of Medical Evangelists, Los Angeles, May 12, Dr. Newton Evans was the faculty guest of honor in recognition of his years of effort to raise the standard of scientific training in the school. The Woman's Auxiliary prepared the picnic dinner; there was a ball game and other entertainment. Prizes were offered. The chairman of the entertainment committee was Dr. Theodore S. Kimball.

### Prize at the University of Kansas

The A. Morris Ginsberg Prize of $100 is given annually to the junior student at the University of Kansas School of Medicine, Kansas City, who shows the highest proficiency in the medical courses of the third year.

### Michigan Premedical Students Organize

A group of premedical students at the University of Michigan, Ann Arbor, organized the University Premedical Society, March 27, electing Vahan A. Kalajan, a junior from Brooklyn, president of the group; John R. C. Adams, Ann Arbor, vice president, and L. J. Fink, Detroit, secretary.

### The Judd Lecture at Minnesota

The seventh annual E. Starr Judd lecture at the University of Minnesota, Minneapolis, was given, March 14, by Dr. Edward D. Churchill, John Homans professor of surgery at Harvard Medical School, Boston, on "Surgery of the Lungs."

### Fellowships Available at Yale

Following are some of the fellowships available at Yale University School of Medicine, New Haven, Conn.:

The William Harvey Cushing Memorial Fellowship, for research in surgery.

The Charles Linnaeus Ives Fellowship, for research in pathology.

The Knight Memorial Fellowship, for research in nervous and mental diseases.

### Student Health

The Student Health Service at Long Island College of Medicine, Brooklyn, is sponsoring a series of talks on health problems to the students, the first of which was delivered by Dr. Arthur W. Grace, professor of dermatology, on "Athlete's Foot and Acne," and the second by Dr. Alfred P. Ingegno of the Student Health Service, who addressed the junior class on "Tuberculosis Among Medical Students."

### Honorary Biological Society

Dr. Francis E. LeJeune, professor of otolaryngology, Tulane University of Louisiana School of Medicine, New Orleans, addressed the Lampyrids, honorary biologic society, recently in the Newcomb administration building on "The "Significance of Hoarseness," illustrated with moving pictures. Sixteen new members have been elected to the Lampyrids from the advanced courses in biology at Newcomb.

### Boston Chapter of Student Association

The Boston University chapter of the Association of Medical Students was recently addressed by Dr. William Barry Wood Jr., Baltimore, on "The Treatment of Pneumococcic Pneumonia." Every Friday noon the Visual Education Committee of this chapter presents medical films with comments by physicians from nearby hospitals; on March 8 the film was entitled "Lumbar Sympathectomy"; on March 15, "Cesarean Section," and on March 22, "Modern Surgical Treatment of Varicose Veins."

### Michigan Internship Appointments

The majority of the members of the senior class of the University of Michigan Medical School, Ann Arbor, have made final arrangements for their internships. Twenty-two members will intern in the University Hospital in Ann Arbor, thirty-two in Detroit, seven each in Grand Rapids and Eloise, and thirteen elsewhere in Michigan, eight each in New York and Ohio, five in Illinois, three in Pennsylvania, two each in California, Texas, Wisconsin and the U. S. Public Health Service, and one in the U. S. Army.

### Dr. Bailey Lectures to Illinois Students

The Illinois chapter of the Association of Medical Students sponsored a lecture at the University of Illinois College of Medicine, Chicago, February 14, by Dr. Percival Bailey, recently appointed professor of neurology and neurologic surgery. His subject was "The Development of Neurology." Dr. Bailey comes to Illinois from the University of Chicago, where he had been professor of neurology since 1928, previous to which time he had worked with Dr. Harvey Cushing in Boston.

### Prize Available at Louisville

The Henry Enos Tuley Memorial Prize is available to the undergraduate at the University of Louisville School of Medicine who submits the best essay on "The Ideals of Medicine." The prize consists of the income from $1,050 subscribed by friends of the late Dean Tuley and is awarded annually at commencement.

### Society to Interest Students in Research

The Research Society of the Long Island College of Medicine, Brooklyn, held its final meeting for the year on April 10. The society serves as a medium for the presentation of original investigations by members of the teaching staff of the college and to interest the students in research. This meeting was addressed by Dr. William S. Tillett of the Department of Medicine, New York University College of Medicine, on "Special Immunological Phenomena Occurring During the Acute Phase of Infections."

### Until September

The Student Section will not be published during June, July and August.